=> file medline FILE 'MEDLINE' ENTERED AT 12:45:34 ON 30 MAY 2002

FILE LAST UPDATED: 29 MAY 2002 (20020529/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> D QUE	L7				
L1 (345096) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	BASE SEQUENCE+NT/CT
L2 (17591) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	CONSERVED SEQUENCE+NT/CT
L3 (17966) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	TRYPSIN INHIBITORS+NT, PFT/CT
	OR 2	ALPHA 1-ANTIT	RYPSIN/C	T	
L4 (10318) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L3/MAJ
L5 (6673) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L4 AND HUMAN/CT
L6 (268) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L5 AND L1
L7	2 SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L6 AND L2
=> D QUE					
T8 (FILE=MEDLINE		PLU=ON	CONSENSUS SEQUENCE/CT
L9 (FILE=MEDLINE		PLU=ON	TRYPSIN INHIBITORS+NT, PFT/CT
	OR 2	ALPHA 1-ANTIT	RYPSIN/C		
L10 (10318) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L9/MAJ
L11 (6673) SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L10 AND HUMAN/CT
L12	0 SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L11 AND L8
					·
=> D QUE			•		
L13 (•	FILE=MEDLINE		PLU=ON	BASE SEQUENCE+NT/CT
		FILE=MEDLINE		PLU=ON	SEQUENCE HOMOLOGY+NT/CT
L15 (FILE=MEDLINE		PLU=ON	TRYPSIN INHIBITORS+NT, PFT/CT
		ALPHA 1-ANTIT			
L16 (•	FILE=MEDLINE			L15/MAJ
L17 (FILE=MEDLINE		PLU=ON	L16 AND HUMAN/CT
L18 (FILE=MEDLINE			L17 AND L13
L19 (FILE=MEDLINE			L14/MAJ
L20	2 SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L18 AND L19
=> D QUE					
L21 (BASE SEQUENCE+NT/CT
L22 (•	FILE=MEDLINE	ABB=ON	PLU=ON	NUCLEIC ACID HYBRIDIZATION+NT/
	CT				

```
86834) SEA FILE=MEDLINE ABB=ON PLU=ON SEQUENCE HOMOLOGY+NT/CT
L23 (
         17966) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT, PFT/CT
L24 (
                 OR ALPHA 1-ANTITRYPSIN/CT
        11446)SEA FILE=MEDLINE ABB=ON PLU=ON L24 AND HUMAN/CT
L25 (
           362)SEA FILE=MEDLINE ABB=ON PLU=ON L25 AND L21
L26 (
            29) SEA FILE=MEDLINE ABB=ON PLU=ON L26 AND L22
L27 (
               5 SEA FILE=MEDLINE ABB=ON PLU=ON L27 AND L23
L28
=> D QUE L33
L29 ( 17591) SEA FILE=MEDLINE ABB=ON PLU=ON CONSERVED SEQUENCE+NT/CT
        30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT
L30 (
         119) SEA FILE=MEDLINE ABB=ON PLU=ON L30 (L) AI/CT
L31 (
            54) SEA FILE=MEDLINE ABB=ON PLU=ON L31 AND HUMAN/CT
L32 (
              0 SEA FILE=MEDLINE ABB=ON PLU=ON L32 AND L29
L33
=> D QUE L38
L34 ( 80566) SEA FILE=MEDLINE ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT/
                  CT
           30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT
L35 (
          119) SEA FILE=MEDLINE ABB=ON PLU=ON L35 (L) AI/CT
L36 (
            54) SEA FILE=MEDLINE ABB=ON PLU=ON L36 AND HUMAN/CT
L37 (
              0 SEA FILE=MEDLINE ABB=ON PLU=ON L37 AND L34
L38
=> D QUE L43
L39 ( 86834) SEA FILE=MEDLINE ABB=ON PLU=ON SEQUENCE HOMOLOGY+NT/CT
           30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT
L40 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRIPSINTPIT/CL
L41 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L40 (L) AI/CT
L42 ( 54) SEA FILE=MEDLINE ABB=ON PLU=ON L41 AND HUMAN,
L40 (
            54) SEA FILE=MEDLINE ABB=ON PLU=ON L41 AND HUMAN/CT
L42 (
               0 SEA FILE=MEDLINE ABB=ON PLU=ON L42 AND L39
L43
 => D QUE L48
            17966) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT, PFT/CT
                  OR ALPHA 1-ANTITRYPSIN/CT
            30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT
L45 (
           119) SEA FILE=MEDLINE ABB=ON PLU=ON L45 (L) AI/CT
 L46 (
             54) SEA FILE=MEDLINE ABB=ON PLU=ON L46 AND HUMAN/CT
 L47 (
              11 SEA FILE=MEDLINE ABB=ON PLU=ON L47 AND L44
 L48
 => D OUE L54
 L49 ( 17966) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT, PFT/CT
                   OR ALPHA 1-ANTITRYPSIN/CT
 L50 ( 10318) SEA FILE=MEDLINE ABB=ON PLU=ON L49/MAJ
L51 ( 6673) SEA FILE=MEDLINE ABB=ON PLU=ON L50 AND HUMAN/CT
L52 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT
L53 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L52 (L) AI/CT
L54 5 SEA FILE=MEDLINE ABB=ON PLU=ON L51 AND L53
```

=> S L7 OR L20 OR L28 OR L48 OR L54 L205 20 L7 OR L20 OR L28 OR L48 OR L54

=> FILE CAPLUS FILE 'CAPLUS' ENTERED AT 12:48:45 ON 30 MAY 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 30 May 2002 VOL 136 ISS 22 FILE LAST UPDATED: 29 May 2002 (20020529/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> D QUE L58
      4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L55 (
          302) SEA FILE=CAPLUS ABB=ON PLU=ON L55 (L) HUMAN
           113) SEA FILE=CAPLUS ABB=ON PLU=ON SEQUENCE HOMOLOGY ANALYSIS+PFT/
L57 (
             O SEA FILE=CAPLUS ABB=ON PLU=ON L56 AND L57
L58
=> D QUE L62
          4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L59 (
           302) SEA FILE=CAPLUS ABB=ON PLU=ON L59 (L) HUMAN
L60 (
          20207) SEA FILE=CAPLUS ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT, P
L61 (
               FT/CT
              1 SEA FILE=CAPLUS ABB=ON PLU=ON L60 AND L61
L62
=> D OUE L64
       4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L63 (
            4 SEA FILE=CAPLUS ABB=ON PLU=ON L63 AND HUMAN/CT
L64
=> D QUE L68
            113) SEA FILE=CAPLUS ABB=ON PLU=ON SEQUENCE HOMOLOGY ANALYSIS+PFT/
L65 (
                CT
                                       PLU=ON
                                               TRYPSIN+PFT/CT
          16881) SEA FILE=CAPLUS ABB=ON
L66 (
                                       PLU=ON L66 AND HUMAN/CT
             42) SEA FILE=CAPLUS ABB=ON
L67 (
                                       PLU=ON L67 AND L65
              O SEA FILE=CAPLUS ABB=ON
L68
=> D QUE L72
          20207) SEA FILE=CAPLUS ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT, P
L69 (
                FT/CT
                                               TRYPSIN+PFT/CT
          16881) SEA FILE=CAPLUS ABB=ON PLU=ON
L70 (
                                               L70 AND HUMAN/CT
             42) SEA FILE=CAPLUS ABB=ON PLU=ON
L71 (
                                       PLU=ON L71 AND L69
              2 SEA FILE=CAPLUS ABB=ON
L72
```

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=> D QUE L74
L73 ( 4667) SEA FILE=CAPLUS ABB=ON PLU=ON PROTEINASE INHIBITOR+PFT/CT
             1 SEA FILE=CAPLUS ABB=ON PLU=ON L73 AND NHP/OBI
=> D QUE L81
        4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L75 (
            113) SEA FILE=CAPLUS ABB=ON PLU=ON SEQUENCE HOMOLOGY ANALYSIS+PFT/
L76 (
                  CT
           16881) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN+PFT/CT
L77 (
           3233) SEA FILE=CAPLUS ABB=ON PLU=ON L77 (L) (ANTAGONI? OR INHIBIT?)
L78 (
           7368) SEA FILE=CAPLUS ABB=ON PLU=ON L75 OR L78
L79 (
             8) SEA FILE=CAPLUS ABB=ON PLU=ON L79 AND MAMMAL/CT
L80 (
                O SEA FILE=CAPLUS ABB=ON PLU=ON L76 AND L80
L81
=> D OUE L88
           4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L82 (
           20207) SEA FILE=CAPLUS ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT, P
L83 (
                  FT/CT
           16881) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN+PFT/CT
L84 (
            3233) SEA FILE=CAPLUS ABB=ON PLU=ON L84 (L) (ANTAGONI? OR INHIBIT?)
L85 (
            7368) SEA FILE=CAPLUS ABB=ON PLU=ON L82 OR L85
L86 (
            8)SEA FILE=CAPLUS ABB=ON PLU=ON L86 AND MAMMAL/CT
L87 (
               O SEA FILE=CAPLUS ABB=ON PLU=ON L87 AND L83
L88
=> D QUE L92
L89 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
            113) SEA FILE=CAPLUS ABB=ON PLU=ON SEQUENCE HOMOLOGY ANALYSIS+PFT/
L90 (
              23) SEA FILE=CAPLUS ABB=ON PLU=ON L89 (L) MAMMA?
L91 (
               O SEA FILE=CAPLUS ABB=ON PLU=ON L91 AND L90
L92
=> D QUE L96
           4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L93 (
            20207) SEA FILE=CAPLUS ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT, P
               23) SEA FILE=CAPLUŚ ABB=ON PLU=ON L93 (L) MAMMA?
L95 (
               O SEA FILE=CAPLUS ABB=ON PLU=ON L95 AND L94
L96
 => D QUE L106
L97 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT
L98 ( 302) SEA FILE=CAPLUS ABB=ON PLU=ON L97 (L) HUMAN
L99 ( 4) SEA FILE=CAPLUS ABB=ON PLU=ON L97 AND HUMAN/CT
L100 ( 16881) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN+PFT/CT
L101 ( 3233) SEA FILE=CAPLUS ABB=ON PLU=ON L100 (L) (ANTAGONI? OR
                   INHIBIT?)
             7368) SEA FILE=CAPLUS ABB=ON PLU=ON L97 OR L101
 L102(
               8) SEA FILE=CAPLUS ABB=ON PLU=ON L102 AND MAMMAL/CT
 L103(
              23) SEA FILE=CAPLUS ABB=ON PLU=ON L97 (L) MAMMA?

325) SEA FILE=CAPLUS ABB=ON PLU=ON L98 OR L99 OR L103 OR L104

7 SEA FILE=CAPLUS ABB=ON PLU=ON L105 AND (HOMOLOG?/OBI OR
 L104(
 L105(
 L106
                   ORTHOLOG?/OBI OR PARALOG?/OBI OR SEQUENCE/OBI (W) SIMILARITY/OB
```

=> S L62 OR L64 OR L72 OR L74 OR L106 L206 14 L62 OR L64 OR L72 OR L74 OR L106

=> FILE EMBASE

FILE 'EMBASE' ENTERED AT 12:51:49 ON 30 MAY 2002 COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE COVERS 1974 TO 23 May 2002 (20020523/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> D QUE L107(L108(L109(L110(L111	3032) SEA 15195) SEA 10579) SEA 4459) SEA	FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE	ABB=ON ABB=ON ABB=ON	PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON	TRYPSIN INHIBITOR+NT, PFT/CT L108 /MAJ L109 AND HUMAN/CT
L113 (L114 (L115 (L116 (75645) SEA 41190) SEA 15195) SEA 10579) SEA 4459) SEA	FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE	ABB=ON ABB=ON ABB=ON	PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON	L116 AND L112
L121(54) SEA 15195) SEA 10579) SEA	FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE	ABB=ON ABB=ON	PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON	TRYPSIN INHIBITOR+NT, PFT/CT L120 /MAJ
=> D QUE L124 (L125 (L126 (L127 (L128	3032) SEA 15195) SEA	FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE	ABB=ON	PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON	TRYPSIN INHIBITOR+NT, PFT/CT L125 (L) EC/CT
L130(L131(L132(75645) SEA 41190) SEA 15195) SEA 2307) SEA 1823) SEA 19) SEA	FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE FILE=EMBASE	ABB=ON ABB=ON ABB=ON ABB=ON ABB=ON	PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON PLU=ON	NUCLEOTIDE SEQUENCE+PFT/CT SEQUENCE HOMOLOGY+PFT/CT TRYPSIN INHIBITOR+NT,PFT/CT L131 (L) EC/CT L132 AND HUMAN/CT L133 AND L129 L134 AND L130

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=> D QUE L140
           54) SEA FILE=EMBASE ABB=ON PLU=ON ORTHOLOGY+PFT/CT
L136(
         15195) SEA FILE=EMBASE ABB=ON PLU=ON TRYPSIN INHIBITOR+NT, PFT/CT
L137(
        2307) SEA FILE=EMBASE ABB=ON PLU=ON L137 (L) EC/CT
L138(
          1823) SEA FILE=EMBASE ABB=ON PLU=ON L138 AND HUMAN/CT
L139(
           O SEA FILE=EMBASE ABB=ON PLU=ON L139 AND L136
L140
=> D OUE L148
         63010) SEA FILE=EMBASE ABB=ON PLU=ON PROTEINASE INHIBITOR+NT/CT
         75645) SEA FILE=EMBASE ABB=ON PLU=ON NUCLEOTIDE SEQUENCE+PFT/CT
L142(
          685) SEA FILE=EMBASE ABB=ON PLU=ON L141 AND L142
L143(
       39777)SEA FILE=EMBASE ABB=ON PLU=ON L141/MAJ
L144(
          408) SEA FILE=EMBASE ABB=ON PLU=ON L144 AND L142
L145(
           54) SEA FILE=EMBASE ABB=ON PLU=ON ORTHOLOGY+PFT/CT
L146(
             1) SEA FILE=EMBASE ABB=ON PLU=ON L143 AND L146
L147(
             O SEA FILE=EMBASE ABB=ON PLU=ON L145 AND L147
L148
=> S L111 OR L118 OR L128 OR L135
            7 L111 OR L118 OR L128 OR L135
=> FILE USPATFUL
FILE 'USPATFULL' ENTERED AT 12:57:03 ON 30 MAY 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 28 May 2002 (20020528/PD)
FILE LAST UPDATED: 28 May 2002 (20020528/ED)
HIGHEST GRANTED PATENT NUMBER: US6397388
HIGHEST APPLICATION PUBLICATION NUMBER: US2002062508
CA INDEXING IS CURRENT THROUGH 28 May 2002 (20020528/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 28 May 2002 (20020528/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2002
>>> USPAT2 is now available. USPATFULL contains full text of the
                                                                      <<<
>>> original, i.e., the earliest published granted patents or
                                                                      <<<
>>> applications. USPAT2 contains full text of the latest US
                                                                      <<<
>>> publications, starting in 2001, for the inventions covered in
                                                                     <<<
>>> USPATFULL. A USPATFULL record contains not only the original
                                                                     <<<
>>> published document but also a list of any subsequent
                                                                      <<<
>>> publications. The publication number, patent kind code, and
                                                                      <<<
>>> publication date for all the US publications for an invention
>>> are displayed in the PI (Patent Information) field of USPATFULL
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.
>>> USPATFULL and USPAT2 can be accessed and searched together
                                                                      <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to
                                                                      <<<
                                                                      <<<
>>> enter this cluster.
>>>
>>> Use USPATALL when searching terms such as patent assignees,
>>> classifications, or claims, that may potentially change from
>>> the earliest to the latest publication.
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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> D QUE L150

```
35) SEA FILE-USPATFULL ABB-ON PLU-ON (TRYPSIN/TI (3A) (INHIBIT?/T
L149(
                I OR ANTAGONI?/TI))
               3 SEA FILE=USPATFULL ABB=ON PLU=ON L149 AND (MAMMA?/TI OR
L150
              HUMAN/TI)
=> D QUE L154
          38417) SEA FILE=USPATFULL ABB=ON PLU=ON (MAMMA?/AB OR HUMAN/AB)
L151(
           139) SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/AB (3A) (INHIBIT?/A
L152(
                 B OR ANTAGONI?/AB))
          52456) SEA FILE-USPATFULL ABB-ON PLU-ON (ORTHOLOG?/AB OR HOMOLOG?/AB
L153(
                  OR SIMILAR?/AB OR IDENTITY/AB OR PARALOG?/AB)
               4 SEA FILE-USPATFULL ABB=ON PLU=ON L151 AND L152 AND L153
L154
=> D OUE L160
L155 ( 1012) SEA FILE=USPATFULL ABB=ON PLU=ON ((PROTEINASE/AB OR PROTEASE/
                 AB) (3A) (INHIBIT?/AB OR ANTAGONI?/AB))
          38417) SEA FILE=USPATFULL ABB=ON PLU=ON (MAMMA?/AB OR HUMAN/AB)
356) SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/AB)
16) SEA FILE=USPATFULL ABB=ON PLU=ON L155 AND L157 AND L156
50684) SEA FILE=USPATFULL ABB=ON PLU=ON SEQUENC?/AB
3 SEA FILE=USPATFULL ABB=ON PLU=ON L158 AND L159
L156(
L157(
L158(
L159(
L160
=> D QUE L168
L161( 1842944) SEA FILE=USPATFULL ABB=ON PLU=ON ORTHOLOG? OR HOMOLOG? OR
                 SIMILAR? OR IDENTITY OR PARALOG?
            1012) SEA FILE=USPATFULL ABB=ON PLU=ON ((PROTEINASE/AB OR PROTEASE/
L162(
                 AB) (3A) (INHIBIT?/AB OR ANTAGONI?/AB))
           38417) SEA FILE=USPATFULL ABB=ON PLU=ON (MAMMA?/AB OR HUMAN/AB)
L163(
           356) SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/AB)
L164(
             16) SEA FILE-USPATFULL ABB-ON PLU-ON L162 AND L164 AND L163
L165(
             14) SEA FILE=USPATFULL ABB=ON PLU=ON L165 AND L161
L166(
           12008) SEA FILE=USPATFULL ABB=ON PLU=ON (PROTEIN OR PEPTIDE) / TI
L167(
               2 SEA FILE-USPATFULL ABB-ON PLU-ON L166 AND L167
L168
=> S L150 OR L154 OR L160 OR L168
             12 L150 OR L154 OR L160 OR L168
L208
=> FILE WPIDS
FILE 'WPIDS' ENTERED AT 12:59:47 ON 30 MAY 2002
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FILE LAST UPDATED: 28 MAY 2002 <20020528/UP>
MOST RECENT DERWENT UPDATE 200234 <200234/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

- >>> The BATCH option for structure searches has been enabled in WPINDEX/WPIDS and WPIX >>>
- >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>
- >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
 SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<
- >>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX TOOLS OF THE TRADE USER GUIDE, PLEASE VISIT:

http://www.derwent.com/data/stn3.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER

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GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<
=> D OUE L173
            781) SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR
L169(
               ANTAG?)
         133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?
L170(
             74) SEA FILE-WPIDS ABB-ON PLU-ON L169 (3A) L170
L171(
          11423) SEA FILE=WPIDS ABB=ON PLU=ON HOMOLOG? OR ORTHOLOG? OR
L172(
                PARALOG? OR SEQUENCE (W) SIMILARITY
              1 SEA FILE=WPIDS ABB=ON PLU=ON L171 AND L172
L173
=> D QUE L180
            781) SEA FILE-WPIDS ABB-ON PLU-ON TRYPSIN (3A) (INHIBIT? OR
L174(
                ANTAG?)
         133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?
Ti175 (
          11423) SEA FILE=WPIDS ABB=ON PLU=ON HOMOLOG? OR ORTHOLOG? OR
L176(
                PARALOG? OR SEQUENCE (W) SIMILARITY
L177(
          27100) SEA FILE=WPIDS ABB=ON PLU=ON
                                              (NUCLEOTIDE OR NUCLEIC OR DNA
                OR RNA OR GENETIC OR CHROMOSOMAL) (3A) SEQUENC?
            168) SEA FILE=WPIDS ABB=ON PLU=ON L174 (S) L175
L178(
             8) SEA FILE=WPIDS ABB=ON PLU=ON L178 AND L176
L179(
              7 SEA FILE-WPIDS ABB-ON PLU-ON L179 AND L177
L180
=> D QUE L185
            781) SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR
L181(
                ANTAG?)
         133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?
L182(
             74) SEA FILE-WPIDS ABB-ON PLU-ON L181 (3A) L182
L183(
          27100) SEA FILE-WPIDS ABB-ON PLU-ON (NUCLEOTIDE OR NUCLEIC OR DNA
L184(
                OR RNA OR GENETIC OR CHROMOSOMAL) (3A) SEQUENC?
              2 SEA FILE=WPIDS ABB=ON PLU=ON L183 AND L184
L185
=> D QUE L189
            781) SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR
L186(
                ANTAG?)
         133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?
L187(
            74) SEA FILE=WPIDS ABB=ON PLU=ON L186 (3A) L187
L188(
              1 SEA FILE-WPIDS ABB-ON PLU-ON L188 AND CDNA
L189
=> D QUE L193
            781) SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR
L190(
                ANTAG?)
         133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?
L191(
            168) SEA FILE=WPIDS ABB=ON PLU=ON L190 (S) L191
L192(
              4 SEA FILE=WPIDS ABB=ON PLU=ON L192 AND CDNA
L193
=> D QUE L198
            781) SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR
L194(
                ANTAG?)
         133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?
L195(
L196(
             74) SEA FILE=WPIDS ABB=ON PLU=ON L194 (3A) L195
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L197(17730) SEA FILE=WPIDS ABB=ON PLU=ON HYBRIDIZ? OR HYBRIDIS? 1 SEA FILE=WPIDS ABB=ON PLU=ON L196 AND L197 L198

=> D QUE L203

L199(781) SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR

ANTAG?)

L200(133029) SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA? 168) SEA FILE=WPIDS ABB=ON PLU=ON L199 (S) L200 L201(

L202(17730) SEA FILE=WPIDS ABB=ON PLU=ON HYBRIDIZ? OR HYBRIDIS?

L203 6 SEA FILE-WPIDS ABB-ON PLU-ON L201 AND L202

=> S L173 OR L180 OR L185 OR L189 OR L193 OR L198 OR L203

15 L173 OR L180 OR L185 OR L189 OR L193 OR L198 OR L203

=> DUP REM L205-209

FILE 'MEDLINE' ENTERED AT 13:04:14 ON 30 MAY 2002

FILE 'CAPLUS' ENTERED AT 13:04:14 ON 30 MAY 2002

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FILE 'USPATFULL' ENTERED AT 13:04:14 ON 30 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 13:04:14 ON 30 MAY 2002

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PROCESSING COMPLETED FOR L205

PROCESSING COMPLETED FOR L206

PROCESSING COMPLETED FOR L207

PROCESSING COMPLETED FOR L208

PROCESSING COMPLETED FOR L209

67 DUP REM L205-209 (1 DUPLICATE REMOVED)

=> D IBIB AB 1-67

L210 ANSWER 1 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:256312 CAPLUS

DOCUMENT NUMBER:

136:289989

TITLE:

Protein and cDNA sequences of a novel human trypsin

sequence homolog and uses thereof

INVENTOR(S):

Meyers, Rachel A.

PATENT ASSIGNEE(S):

Millennium Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002026802 A2 20020404 WO 2001-US29904 20010924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

```
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
              PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                             US 2000-235023P P 20000925
PRIORITY APPLN. INFO.:
     The invention provides protein and cDNA sequences of a novel human
     protein, designated m32404, which has sequence homol. with trypsin
     members. The invention also provides antisense nucleic acid mols.,
     recombinant expression vectors contg. m32404 nucleic acid mols., host
     cells into which the expression vectors have been introduced, and nonhuman
     transgenic animals in which an m32404 gene has been introduced or
     disrupted. The invention still further provides isolated m32404 proteins,
     fusion proteins, antigenic peptides and anti-m32404 antibodies.
     Diagnostic methods utilizing compns. of the invention are also provided.
```

L210 ANSWER 2 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:143003 CAPLUS

DOCUMENT NUMBER:

136:180179

TITLE: INVENTOR(S): Methods for ultra-sensitive detection systems

Chait, Brian T.; Latimer, Darin R.; Lizardi, Paul M.;

Kershnar, Eric R.; Morrow, Jon S.; Roth, Matthew E.; Mattessich, Martin J.; McConnel, Kevin J.

PATENT ASSIGNEE(S): SOURCE:

Agilix Corporation, USA

PCT Int. Appl., 341 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
APPLICATION NO. DATE
                  KIND DATE
    PATENT NO.
                                       ------
                         _____
    ----- ----
                         20020221 WO 2001-US41709 20010813
                    A2
    WO 2002014867
       W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
           CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
           GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
           LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
            RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
           VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
           DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
           BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                     US 2000-224939P P 20000811
PRIORITY APPLN. INFO.:
                                     US 2001-283498P P 20010412
```

Disclosed are compns. and methods for sensitive detection of one or AB multiple analytes. In general, the methods involve the use of special label components, referred to as reporter signals, that can be assocd. with, incorporated into, or otherwise linked to the analytes. In some embodiments, the reporter signals can be altered such that the altered forms of different reporter signals can be distinguished from each other. In some embodiments, sets of reporter signals can be distinguished from each other. In some embodiments, sets of reporter signals can be used where two or more of the reporter signals in a set have one or more common properties that allow the reporter signals having the common property to be distinguished and/or sepd. from other mols. lacking the common property. In other embodiments, sets of reporter signal/analyte conjugates can be used where two or more of the reporter signal/analyte

conjugates in a set have one or more common properties that allow the reporter signal/analyte conjugates having the common property to be distinguished and/or sepd. form other mols. lacking the common property. Reporter signals can also be in conjunction with analytes (such as in mixts. of reporter signals and analytes), where no significant phys. assocn. between the reporter signals and analytes occurs; or alone, where no analyte is present.

L210 ANSWER 3 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:51264 CAPLUS

DOCUMENT NUMBER: 136:112690

TITLE: Method of modulating expression of

LDL-receptor-related protein and uses thereof

INVENTOR (S): Partridge, Nicola

PATENT ASSIGNEE(S): Saint Louis University, USA

PCT Int. Appl., 67 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
PATENT NO.
                                          APPLICATION NO. DATE
                     KIND DATE
     -----
                                           -----
                                          WO 2001-US18919 20010613
     WO 2002003985
                      A1
                            20020117
         SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                        US 2000-612533
                                                        A 20000707
     Methods for increasing expression of the LDL receptor-related protein
AΒ
     (LRP) in cells or animals are disclosed. The methods comprise treating
     the cells or animals with an HMG-CoA reductase inhibitor (statin). Such
     treatments are also useful for: reducing activity of LRP ligands in cells
     or animals, detg. whether a particular condition is caused by insufficient
     or excess expression of an LRP, detg. whether a particular protein is
     inactivated by an LRP, and other similar applications. More specifically,
     the invention relates to the enhancement of levels of LRP in cells and
     animals and uses thereof in treating disorders mediated by excessive
     levels of proteins which bind to LRP or have receptors which bind to LRP.
REFERENCE COUNT:
                         5
                               THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

CAPLUS COPYRIGHT 2002 ACS L210 ANSWER 4 OF 67 ACCESSION NUMBER: 2002:284646 CAPLUS

DOCUMENT NUMBER: 136:306664

TITLE: Antistreptococcal agents containing bactericidal

peptides and sterilization of streptococci

INVENTOR (S):

Nishimura, Eisaku; Kato, Masatoshi; Etou, Akiko; Imai,

Susumu; Nishizawa, Toshiki; Hanada, Nobuhiro

PATENT ASSIGNEE(S):

Morinaga and Co., Ltd., Japan Jpn. Kokai Tokkyo Koho, 11 pp. SOURCE:

CODEN: JKXXAF

DOCUMENT TYPE:

Patent Japanese

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

> KIND DATE PATENT NO. APPLICATION NO. DATE

JP 2002114704 A2 20020416 JP 2000-300693 20000929

Streptococci are sterilized using agents contg. antibacterial peptides AB such as human .beta.-defensin-2 and optionally protease inhibitors. The antistreptococcal agents are useful as pharmaceuticals and as food additives. Human .beta.-defensin-2 inhibited growth of Streptococcus gordonii, S. cricetus, S. pyogenes, etc. Combined use of 3,4-dichloroisocoumarin (serine protease inhibitor) enhanced antibacterial activity of human .beta.-defensin-2 on S. anginosus and S. mitis.

L210 ANSWER 5 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-227151 [28] WPIDS

DOC. NO. CPI:

C2002-069183

TITLE:

gcpE nucleic acid which is an essential gene of the methyl-D-erythritol phosphate pathway, encoding a fully defined GCPE protein which is useful for increasing

levels of tocopherol substrates in plants.

DERWENT CLASS:

C06 D16

INVENTOR(S):

BORONAT, A; CAMPOS, N; RODRIGUEZ-CONCEPCION, M; ROHMER,

M; SEEMAN, M; VALENTIN, H E; VENKATESH, T V;

VENKATRAMESH, M

PATENT ASSIGNEE(S):

(MONS) MONSANTO TECHNOLOGY LLC

COUNTRY COUNT:

95

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG _____

WO 2002012478 A2 20020214 (200228)* EN 155

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU

SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO KIND APPLICATION DATE _____ WO 2001-US24335 20010806 WO 2002012478 A2

PRIORITY APPLN. INFO: US 2000-223483P 20000807

WO 200212478 A UPAB: 20020502

NOVELTY - A substantially purified gcpE nucleic acid molecule (an essential gene of methyl-D-erythritol phosphate (MEP) pathway) (I) that encodes rice, Arabidopsis thaliana, rice or Escherichia coliGCPE protein comprising fully defined 686, 740, 603 or 372 amino acids respectively as given in specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a recombinant nucleic acid molecule (II) as operably linked components:
 - (a) an exogenous promoter; and
- (b) a heterologous nucleic acid molecule encoding rice (S2,9,), A. thaliana (S1,5,13-20,), E. Coli (S3,), soybean (S6,33-46), tomato (S7),

Mesembryanthemum crystallinum (S8), maize(S10,21-32), Loblolly pine (S11), Physcomitrella patens (S12), or Brassica napus (S47) GCPE having fully defined 211-33675 nucleotide sequences given in the specification;

- (2) a recombinant nucleic acid molecule (III) comprising as operably linked components:
- (a) a promoter that functions in a plant cell to cause production of an mRNA molecule, and;
- (b) a nucleic acid sequence that hybridizes under moderate stringency conditions to (S1)-(S3), (S5)-(S47) or their complements, i.e., has greater than 85% identity to the above mentioned sequences or their complements;
 - (3) a transformed cell (IV) comprising (II);
- (4) a substantially purified protein (V) comprising an amino acid sequence of (S4), (S48) or (S49);
 - (5) an antibody (VI) that specifically binds to (V);
 - (6) a transgenic plant (VII) comprising (II);
- (7) a transgenic plant (VIII) comprising a nucleic acid molecule that encodes GCPE protein, where the nucleic acid molecule comprises a promoter operably linked to heterologous nucleic acid sequences having a sequence of (S1)-(S3), (S5)-(S47), or their complements;
 - (8) a seed (IX) derived from (VII);
 - (9) oil or meal derived from (IX);
- (10) a container (X) of seeds, where at least 25% of the seeds are derived from (VIII); and
 - (11) feed stock or plant part (XI) derived from (VIII).
- USE (I) having a sequence of (S1)-(S3), (S5)-(S47), and encoding a GCPE protein having a sequence of (S4), (S48)-(S50), is useful for producing a transgenic plant such as Brassica campestris, B.napus, canola, castor bean, coconut, cotton, crambe, linseed, maize, mustard, oil palm, peanut, rapeseed, rice, safflower, sesame, soybean, sunflower, or wheat with an increased isoprenoid (preferably, tocopherol) compound level (claimed). The expression of GCPE protein in organisms increases the level of tocopherol substrate such as isopentyl diphosphate and dimethylallyl diphosphate biosynthesis. Transgenic organisms overexpressing GCPE protein can nutritionally enhance food and feed sources. Overexpression of GCPE protein in transgenic plant may provide tolerance to stresses e.g., oxidative stress tolerance such as to oxygen or ozone, UV tolerance, etc. (I) may be used to obtain nucleic acid molecules from the same species, and to obtain nucleic acid homologs. (I) is also used as or primers. The recombinant vectors are used in plant transformation or transfection. (I) an also act as markers capable of detecting polymorphisms such as single nucleotide polymorphisms (SNPs). (I) is also used to determine the level or pattern of expression the protein. Dwq.0/5

L210 ANSWER 6 OF 67 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2001:636220 CAPLUS

DOCUMENT NUMBER: 135:206487

TITLE: Twelve human polypeptides and their nucleic acids

sequences and diagnostic and therapeutic applications

Vernet, Corine A. M.; Fernandes, Elma; Shimkets, INVENTOR(S):

Richard A.; Macdougall, John; Spaderna, Steven K.

Curagen Corporation, USA

PATENT ASSIGNEE(S): PCT Int. Appl., 189 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
KIND DATE
                                          APPLICATION NO. DATE
     PATENT NO.
     WO 2001062928 A2 20010830 WO 2001-US6151 20010226
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                       US 2000-184951P P 20000225
PRIORITY APPLN. INFO.:
                                        US 2000-185548P P 20000228
                                        US 2000-185967P P 20000301
                                        US 2000-197723P P 20000418
                                        US 2000-199957P P 20000427
                                        US 2001-789390 A2 20010223
     The present invention provides 12 novel human NOVX polynucleotides and
AΒ
     polypeptides encoded by the NOVX polynucleotides. Three of the proteins
     are novel KIAA1233-like polypeptides; four are STE20-like splice variant
     polypeptides; and five are trypsin inhibitor-like polypeptides. Quant.
     expression anal. in various cells and tissues suggest that these
     polypeptide and cDNA mols. may be of value for the diagnosis and treatment
     of cancer or inflammation conditions. Also provided are the antibodies
     that immunospecifically bind to a NOVX polypeptide or any deriv., variant,
     mutant or fragment of the NOVX polypeptide, polynucleotide or antibody.
     The invention addnl. provides methods in which the NOVX polypeptide,
     polynucleotide and antibody are utilized in the detection and treatment of
     a broad range of pathol. states, as well as to other uses.
L210 ANSWER 7 OF 67 CAPLUS COPYRIGHT 2002 ACS
                         2001:228919 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         134:247996
                         Protein and cDNA sequences for a novel human protease
TITLE:
                         inhibitor-like protein NHP and use thereof
                         Donoho, Gregory; Turner, C. Alexander, Jr.; Wattler,
INVENTOR(S):
                         Frank; Nehls, Michael; Friedrich, Glenn; Zambrowicz,
                         Brian; Sands, Arthur T.
PATENT ASSIGNEE(S):
                         Lexicon Genetics Incorporated, USA
SOURCE:
                         PCT Int. Appl., 29 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                                         APPLICATION NO. DATE
     PATENT NO. KIND DATE
     PATENT NO.
                                          ------
     WO 2001021651 A2 20010329
WO 2001021651 A3 20020314
                            20010329
                                         WO 2000-US26048 20000922
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 1999-156101P P 19990924 PRIORITY APPLN. INFO.:

The invention provides protein and cDNA sequences for a novel human protease inhibitor-like protein NHP that can be used in therapeutic, diagnostic, and pharmacogenomic applications.

L210 ANSWER 8 OF 67 USPATFULL

ACCESSION NUMBER:

2001:163313 USPATFULL

TITLE:

INVENTOR (S):

Protein having proteinase inhibitor activity Delaria, Kathy, Walnut Creek, CA, United States Roczniak, Steve, Lafayette, CA, United States

Davies, Christopher, Walnut Creek, CA, United States

PATENT ASSIGNEE(S):

Bayer Corporation, Berkeley, CA, United States (U.S.

corporation)

KIND DATE NUMBER _____ ____ US 6294648 B1 20010925 US 1999-358569 19990720 PATENT INFORMATION: 19990720 (9)

APPLICATION INFO .: DOCUMENT TYPE:

Utility GRANTED

FILE SEGMENT: PRIMARY EXAMINER:

Nashed, Nashaat T. ASSISTANT EXAMINER: Fronda, Christian L

NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT:

1188

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

BTL.009 is a novel human serine proteinase

inhibitor of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase, and chymotrypsin than towards trypsin-like proteinases. BTL.009, or variants thereof, may be employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

L210 ANSWER 9 OF 67 USPATFULL

ACCESSION NUMBER:

2001:14463 USPATFULL

TITLE:

INVENTOR(S):

Protein having proteinase inhibitor activity

Davies, Christopher, 265 San Antonio Way, Walnut Creek,

CA, United States 94598

Chen, Dadong, 2123 Clinton Ave., #A, Alameda, CA,

United States 94501

Roczniak, Steve, 11 Hidden Valley Rd., Lafayette, CA,

United States 94549

NUMBER KIND DATE _____ PATENT INFORMATION:

APPLICATION INFO .:

US 6180607 B1 20010130 US 1999-369494 19990805 (9)

Utility DOCUMENT TYPE: Granted FILE SEGMENT: PRIMARY EXAMINER: ASSISTANT EXAMINER:

Wax, Robert A. Kerr, Kathleen M.

LEGAL REPRESENTATIVE: Beck, Michael J. NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1,11 1175 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

BTL.010 is a novel human serine proteinase AB inhibitor of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase-, and proteinase 3, than towards trypsin-like proteinases. BTL.010, or variants thereof, may be employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

L210 ANSWER 10 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-582099 [65] WPIDS

DOC. NO. NON-CPI:

N2001-433669

DOC. NO. CPI:

C2001-172594

TITLE:

New stable chloroplast expression vector for introducing multiple genes into a plant by a single integration event, comprises a multi-gene operon which is functional

to co-express multiple enzymes in plastids.

DERWENT CLASS:

C06 D16 P13

INVENTOR(S):

DANIELL, H; MOAR, W

PATENT ASSIGNEE(S): (AUBU) UNIV AUBURN; (UYFL-N) UNIV CENT FLORIDA

COUNTRY COUNT:

95

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG ______

WO 2001064024 A1 20010907 (200165)* EN 72

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001045360 A 20010912 (200204)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 20010640		WO 2001-US6276	20010228
AU 20010453		AU 2001-45360	20010228

FILING DETAILS:

PATENT NO PATENT NO KIND ______ AU 2001045360 A Based on WO 200164024

PRIORITY APPLN. INFO: US 2001-266121P 20010202; US 2000-185660P 20000229; US 2000-257408P 20001220; US 2000-259248P 20001229

WO 200164024 A UPAB: 20011108 AΒ NOVELTY - A stable chloroplast transformation and expression vector (I) which is capable of introducing multiple genes into a plant by a single integration event, comprises a heterologous coding sequence comprising an expression cassette which comprises a promoter operative in plastids, a selectable marker, multi-gene operon which is functional to co-express multiple enzymes in the plastids, is new.

DETAILED DESCRIPTION - A new stable chloroplast transformation and expression vector (I) comprises a heterologous DNA

sequence which comprises an expression cassette, comprising operably linked components, in the 5' to the 3' direction of translation, a promoter operative in the plastids which drives a multi-gene operon, a selectable marker sequence, the multi-gene operon which is functional to co-express multiple enzymes in the plastids, a transcription termination region functional in the plastids, and flanking each side of the expression cassette, flanking DNA sequences which are homologous to DNA sequences inclusive of a

spacer sequence of the target plastid genome, whereby stable integration of the heterologous coding sequence into the chloroplast genome of the target plant is facilitated throughout homologous recombination of the flanking sequence with the homologous sequences in the target plastid gene.

INDEPENDENT CLAIMS are also included for the following:

- (1) transforming (M1) a chloroplast of a selected plant species or its progeny to confer insect resistance and producing foreign protein on a large scale, involving stably transforming the chloroplast of the selected plant cells to express an insecticidal toxic protein and a chaperonin and growing the transformed plant cells under conditions which allow the expression of the insecticidal toxin protein and chaperonin;
 - (2) a transformed plant (II) which has been transformed by (M1);
 - (3) progeny including seeds of (II);
- (4) transforming (M2) a chloroplast of a selected plant species or its progeny to confer greater resistance to metal ions than the corresponding parental plant which does not require several back crosses to create a complete pathway that detoxifies mercury and organomercurial compounds involving stably transforming the chloroplast of a plant by inserting an expression cassette containing (I), where the expression cassette comprises the mercury resistance coding sequences that encode Mer A and Mer B enzymes, into a plant species or its progeny and growing the transforming plant species under conditions which allow the expression of the expression cassette;
- (5) a stably transformed plant (III) which has been transformed by (M2);
 - (6) progeny including seeds of stably transformed (III);
- (7) phytoremediation (M3) which does not require several backcrosses to create a complete pathway that detoxifies mercury and organomercurial comprising (M2);
- (8) a photosynthetic organism (IV) transformed with (I) where the expression cassette comprises genes for a biosynthetic pathway that is a bioremediation system functioning to degrade inorganic and organic mercury compounds, and where (IV) is useful for bioremediation of mercury and organomercuric compounds from contaminated water bodies; and
- (9) transforming (M4) a chloroplast of a selected photosynthetic organism to confer greater resistance to metal ions involving stably transforming chloroplast with (I) where the expression cassette comprises genes for a biosynthetic pathway that is a bioremediation system functioning to degrade inorganic and organic mercury compounds, and growing the transformed photosynthetic organism which allows the expression of the expression cassette.

ACTIVITY - Anti-insecticidal. No biological data is given. MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful in a bioremediation process where its expression cassette comprises operon having genes that function to degrade inorganic compounds such as divalent cations of mercury, nickel, cobalt, trivalent cations of gold, or monovalent cations of silver, and organic compounds such as alkyl mercury, alkenyl mercury, alkynyl mercury, aromatic mercury compounds, alkyl lead compounds, alkyl arsenic compounds or alkyl cadmium compounds. A transformed plant (III) or its progeny including seeds is useful for phytoremediation of mercury and organomercurials in soil and

ground waters. The method involves planting (III) or progeny in soils contaminated with organomercurials and allowing the plants to grow. A photosynthetic organism (IV) transformed with (I) is useful for phytoremediation of mercury and organomercurials in contaminated water which involves treating water contaminated with the mercury with (IV) before releasing the water into the environment. (IV) is a green algae such as Chlorella vulgaris or a cyanobacteria such as Synechocytis (claimed). The vector is useful for genetic engineering of plant cells, preferably for engineering novel pathways for metabolic engineering and gene stacking. The mer operon-expressing plants can be used in remediation of mercury-contaminated soil to block the biomagnification of methyl mercury up the food chain.

ADVANTAGE - The vector provides enhanced expression of several foreign proteins in plastids utilizing a single transformation event. Blocks of foreign genes in the single operon avoids complications inherent in nuclear transformation. Formation of crystals of foreign proteins enables simple purification, and also the folded crystals (e.g., Bacillus thuringiensis (Bt) toxin protein) crystals improve the safety of the Bt transgenic plants. Absence of the insecticidal protein in transgenic pollen eliminates toxicity to non-target insects via pollen. Expression of cry2Aa2 operon in chloroplasts provides a model system for hyper-expression of foreign proteins in a folded configuration enhancing their stability and facilitating single step purification. The metal resistant plants generated by above mentioned methods effectively harvest precious and semi-precious metals and trap them in their plant tissues. 100 fold greater amounts of insecticidal protein can be found in plants co-expressing the chaperon protein versus plants having only the gene encoding the insecticidal protein. Dwg.0/14

L210 ANSWER 11 OF 67 WPIDS (C) 2002 THOMSON DERWENT WPIDS

ACCESSION NUMBER:

2001-147325 [15]

DOC. NO. CPI:

C2001-043631

TITLE:

Recombinant protein derived from ticks that is capable of inhibiting human mast cell tryptase activity, useful for treating and preventing inflammation in humans or animals, and for the depletion or removal of tryptase from a food product.

DERWENT CLASS:

B04 D16

INVENTOR(S):

NUTTALL, P A; PAESEN, G C

PATENT ASSIGNEE(S):

(EVOL-N) EVOLUTEC LTD

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA	PG

WO 2001005823 A2 20010125 (200115) * EN

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000060040 A 20010205 (200128)

BR 2000012589 A 20020409 (200232)

A2 20020417 (200233) EP 1196579

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO K	IND	AP	PLICATION	DATE
WO 2001005823	A2		2000-GB2791	20000719
AU 2000060040			2000-60040	20000719
BR 2000012589	A		2000-12589	20000719
			2000-GB2791	20000719
EP 1196579	A2		2000-946166	20000719
		WO	2000-GB2791	20000719

FILING DETAILS:

PATENT NO	KIND	PA	TENT NO
AU 20000600	40 A Based	on WO	200105823
BR 20000125	89 A Based	on WO	200105823
EP 1196579	A2 Based	on WO	200105823

PRIORITY APPLN. INFO: GB 1999-16913 19990719

AB WO 200105823 A UPAB: 20010317

NOVELTY - A recombinant protein (I), its active fragment or functional equivalent, derived from a blood-feeding arthropod ectoparasite, preferably ticks, that is capable of inhibiting the activity of a human mast cell tryptase, is new.

DETAILED DESCRIPTION - A recombinant protein (I), its active fragment or functional equivalent, derived from a blood-feeding arthropod ectoparasite, preferably ticks, that is capable of inhibiting the activity of a human mast cell tryptase, is new.

(I) exhibits significant sequence **homology** with the tick-derived protease inhibitor protein (TdPI; a 118 amino acid sequence (S1) as defined in the specification), its active fragment or its functional equivalent.

INDEPENDENT CLAIMS are also included for the following:

- (1) a vaccine composition (VC) comprising (I)
- (2) formulating VC, by bringing (I), its fragment or functional equivalent into association with a pharmaceutically acceptable carrier;
 - (3) a nucleic acid molecule (II) encoding (I);
- (4) a nucleic acid molecule (IIa) having the 490 nucleotide sequence defined in the specification which hybridizes with (II) under stringent hybridization conditions, or which encodes (I);
 - (5) a viral vector (III) comprising (II) or (IIa);
 - (6) a host cell (IV) transformed or transfected with (III);
 - (7) a transgenic animal (V) transformed by (II) or (IIa);
 - (8) preparing (I) by culturing (IV); and
- (9) a method for vaccinating a mammal against a disease, or for treating a mammal suffering from a disease, comprising administering (I), its fragment or functional equivalent.

ACTIVITY - Antiinflammatory; antiasthmatic; antipsoriatic; antirheumatoid; antiarthritic; antiallergic; cytostatic.

MECHANISM OF ACTION - Inhibitor of tryptase, preferably human mast cell tryptase; vaccine (claimed); gene therapy.

No supporting biological data given.

USE - (I) is useful as a pharmaceutical and in the manufacture of a medicament for treating inflammation in humans and animals. (I) is useful for treating and preventing inflammation in humans or animals. One or more epitopes of (I) can be used in the development of vaccines that target proteins that exhibit significant sequence homology with TdPI. (I) is useful for vaccinating a mammal against a disease. Bovine colostrum trypsin inhibitor,

Page 20

rat tissue factor pathway inhibitor (TFPI-2), Kunitz domain of tick anticoagulant peptide TAP or the two domains in ornithodorin, are useful as a tryptase inhibitor.

(I) is useful in the detection or quantification of tryptase, for the depletion or removal of tryptase from a food product or from a cell culture, as an anti-tryptase agent or as an antiinflammatory drug (all claimed).

(I) is useful for treating asthma, psoriasis, interstitial lung disease, rheumatoid arthritis, gingivitis, peridontitis, allergic reactions, cancer and any other tryptase-mediated condition. (I) is useful as an immunogen, and as a tool in the study of inflammation, inflammation-related processes, or other physiological processes involving tryptase. VC is useful for vaccinating against a broad range of arthropod and/or helminth genera. Dwg.0/6

L210 ANSWER 12 OF 67 CAPLUS COPYRIGHT 2002 ACS

2001:812153 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

136:65865

TITLE: AUTHOR(S): Deamidation of human proteins Robinson, N. E.; Robinson, A. B.

CORPORATE SOURCE:

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA,

91125, USA

SOURCE:

Proceedings of the National Academy of Sciences of the United States of America (2001), 98(22), 12409-12413

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER:

National Academy of Sciences

DOCUMENT TYPE:

Journal English

LANGUAGE:

Deamidation of asparaginyl and glutaminyl residues causes time-dependent changes in charge and conformation of peptides and proteins. Quant. and exptl. verified predictive calcns. of the deamidation rates of 1,371 asparaginyl residues in a representative collection of 126 human proteins have been performed. These rates suggest that deamidation is a biol.

relevant phenomenon in a remarkably large percentage of human proteins. 36

REFERENCE COUNT:

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L210 ANSWER 13 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2001:520875 CAPLUS

DOCUMENT NUMBER:

136:52537

TITLE:

Interferon-.gamma. in healthy subjects: selective

modulation of inflammatory mediators

AUTHOR (S):

De Metz, J.; Hack, C. E.; Romijn, J. A.; Levi, M.; Out, T. A.; Ten Berge, I. J. M.; Sauerwein, H. P.

CORPORATE SOURCE:

Academic Medical Centre, University of Amsterdam,

Amsterdam, 1100 DE, Neth.

SOURCE:

European Journal of Clinical Investigation (2001),

31(6), 536-543

CODEN: EJCIB8; ISSN: 0014-2972

PUBLISHER:

Blackwell Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

It is suggested that interferon-.gamma. (IFN-.gamma.), like other cytokines, is a mediator in the host inflammatory response, which could be of importance in the pathophysiol. of sepsis. The role of IFN-.gamma. in human host inflammatory responses, however, has not been studied. placebo-controlled trial we studied the acute effects of IFN-.gamma. administration on host inflammatory mediators in healthy men: i.e. the

cytokine/chemokine cascade system, acute-phase proteins, activation markers of the innate cellular immunity and coagulation/fibrinolysis parameters. IFN-.gamma. increased plasma levels of interleukin-6 (IL-6), IL-8 and IFN-.gamma.-inducible protein-10 (IP-10), but did not affect plasma levels of other cytokines (IL-4, IL-10, tumor necrosis factor-.alpha., IL-12p40/p70). Plasma concns. of C-reactive protein and secretory phospholipase A2 both increased. Plasma levels of the leukocyte activation marker elastase-.alpha.1-antitrypsin complexes increased after IFN-.gamma. administration, IFN-.gamma. increased the percentage of high-affinity Fc.gamma.-receptor (Fc.gamma.RI) -pos. neutrophils, but did not affect the mean fluorescence intensity of Fc.gamma.RI on neutrophils. Procoagulant and profibrinolytic effects of IFN-.gamma. were evidenced by increased plasma levels of prothrombin fragment F1 + F2, tissue-plasminogen activator and plasmin-.alpha.2-antiplasmin complexes. Thus, IFN-.gamma. selectively affects host inflammatory mediators in humans.

REFERENCE COUNT:

THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS 55 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L210 ANSWER 14 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:133848 CAPLUS

DOCUMENT NUMBER:

132:190514

Human proteases and associated proteins and cDNAs and TITLE:

their uses in drug screening and therapy

Bandman, Olga; Hillman, Jennifer L.; Baughn, Mariah INVENTOR(S):

R.; Azimzai, Yalda; Guegler, Karl J.; Corley, Neil C.; Yue, Henry; Tang, Y. Tom; Reddy, Roopa; Patterson, Chandra; Au-young, Janice; Shih, Leo L.; Lu, Dyung

Aina M.

Incyte Pharmaceuticals, Inc., USA PATENT ASSIGNEE(S):

PCT Int. Appl., 114 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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APPLICATION NO. DATE
                   KIND DATE
    PATENT NO.
    ______
                                        ______
                   A2
                                       WO 1999-US17818 19990806
    WO 2000009709
                          20000224
                          20000908
    WO 2000009709
                    A3
           AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
            TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
            RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
            ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
            CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                       AU 1999-53403
                                                        19990806
                          20000306
                     A1
    AU 9953403
                                       EP 1999-939042
                     A2
                          20010606
    EP 1104473
          AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
PRIORITY APPLN. INFO.:
                                     US 1998-96114P
                                                     P 19980810
                                     US 1999-119768P P 19990211
                                     WO 1999-US17818 W 19990806
```

The invention provides human proteases and assocd. proteins (PPRGs) and AB polynucleotides which identify and encode PPRG. The invention also provides expression vectors, host cells, antibodies, agonists, and

antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders assocd. with expression of PPRG.

L210 ANSWER 15 OF 67 USPATFULL

ACCESSION NUMBER:

2000:138080 USPATFULL

TITLE:

Recombinant methods for production of serine protease

inhibitors and DNA sequences useful for same

INVENTOR (S):

Bandyopadhyay, Pradip K., Boulder, CO, United States Eisenberg, Stephen P., Boulder, CO, United States Stetler, Gary L., Lafayette, CO, United States Thompson, Robert C., Boulder, CO, United States

PATENT ASSIGNEE(S):

Amgen Boulder Inc., Boulder, CO, United States (U.S.

KIND DATE

corporation)

NUMBER

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.:

______ 20001017 US 6132990 US 1991-712354 19910607 (7)

Division of Ser. No. US 1989-293042, filed on 3 Jan 1989, now abandoned which is a continuation-in-part of

Ser. No. US 1987-82962, filed on 4 Aug 1987, now abandoned And a continuation-in-part of Ser. No. US 1987-31846, filed on 30 Mar 1987, now abandoned And a continuation-in-part of Ser. No. US 1986-890526, filed

on 29 Jul 1986, now abandoned which is a

continuation-in-part of Ser. No. US 1985-803471, filed

on 2 Dec 1985, now abandoned which is a

continuation-in-part of Ser. No. US 1984-678822, filed

on 6 Dec 1984, now abandoned

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER: ASSISTANT EXAMINER: Wax, Robert A. Moore, William W.

LEGAL REPRESENTATIVE:

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

7 Drawing Figure(s); 7 Drawing Page(s)

NUMBER OF DRAWINGS: LINE COUNT:

3196

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A synthetic DNA sequence and its genetic equivalents are disclosed which sequences are capable, when used in a recombinant DNA method, of directing production of a serine protease inibitor protein. Recombinant DNA methods for the production of serine protease inhibitor proteins are also disclosed. These methods incorporate either the synthetic DNA sequence of the present invention or natural DNA sequences isolated from human cDNA or genomic libraries.

In addition, a single polypeptide chain protein is disclosed which is capable of inhibiting chymotrypsin and elastase but not trypsin . In one embodiment, this protein is a shortened from (single domain) of the protein produced by the method described herein.

L210 ANSWER 16 OF 67

WPIDS (C) 2002 THOMSON DERWENT WPIDS

ACCESSION NUMBER:

2000-182719 [16]

DOC. NO. CPI:

C2000-057316

TITLE:

Novel screen comprising a pool of vectors with randomly modified nucleotide sequences, useful

for identifying modulators of enzyme activity useful for

selecting antibiotic agents.

DERWENT CLASS: B04 D13 D15 D16

INVENTOR(S):

HALKIER, T; JENSEN, A; JESPERSEN, L

PATENT ASSIGNEE(S):

(MEBI-N) M & E BIOTECH AS; (PHAR-N) PHARMEXA AS; (INOX-N)

INOXELL AS

COUNTRY COUNT:

87

PATENT INFORMATION:

PG PATENT NO KIND DATE WEEK LA _____

WO 2000005406 A1 20000203 (200016)* EN 136

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU

LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR

TT UA UG US UZ VN YU ZA ZW

AU 9948985 A 20000214 (200029)

EP 1098991 A1 20010516 (200128) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI

NO 2001000300 A 20010319 (200129)

CZ 2001000210 A3 20010613 (200138)

HU 2001002457 A2 20011029 (200175)

SK 2001000069 A3 20011203 (200203)

ZA 2001000195 A 20020327 (200230) 188

KR 2001103560 A 20011123 (200232)

APPLICATION DETAILS:

PATENT NO KIND	APPLICATION	DATE
WO 200005406 A1	WO 1999-DK408	19990716
AU 9948985 A	AU 1999-48985	19990716
EP 1098991 A1	EP 1999-932689	19990716
	WO 1999-DK408	19990716
NO 2001000300 A	WO 1999-DK408	19990716
	NO 2001-300	20010118
CZ 2001000210 A3	WO 1999-DK408	19990716
	CZ 2001-210	19990716
HU 2001002457 A2	WO 1999-DK408	19990716
	HU 2001-2457	19990716
SK 2001000069 A3	WO 1999-DK408	19990716
	SK 2001-69	19990716
ZA 2001000195 A	ZA 2001-195	20010108
KR 2001103560 A	KR 2001-700871	20010119

FILING DETAILS:

PAT	TENT NO K	IND			PAT	TENT NO
AU	9948985	A	Based	on	WO	200005406
EΡ	1098991	A1	Based	on	WO	200005406
CZ	2001000210	А3	Based	on	WO	200005406
HU	2001002457	A2	Based	on	WO	200005406
SK	2001000069	Δ3	Based	on	WO	200005406

PRIORITY APPLN. INFO: US 1998-94868P 19980729; DK 1998-956 19980720

WO 200005406 A UPAB: 20000330

NOVELTY - Cell screen (I) comprising using a pool of expression vectors,

each with one member from a library of randomly modified nucleotide sequence (NS) encoding a scaffold portion of a parent peptide or RNA.

DETAILED DESCRIPTION - The screen (I) identifies an in vivo modulator of a target enzyme by preparing a pool of expression vectors, transforming a population of substantially identical cells harboring the enzyme, culturing the cells and isolating transformed cells where activity of the enzyme is modulated. The modulator is identified by determining a randomly modified vector NS and/or by determining the amino acid (aa) or RNA sequence of the expression product encoded by NS.

INDEPENDENT CLAIMS are also included for the following:

(1) preparation of replicable vector;

(2) cells transformed by the vector of (1);(3) producing an enzyme modulator comprising:

(a) growing a cell as in (2); and

- (b) harvesting the expression product; or
- (c) identifying the modulator according to (I); and

(d) synthesizing the modulator; and

(4) isolating and/or identifying a target biomolecule (M1) using the modulator as an affinity ligand in an affinity purification step, or as a probe against a cDNA library derived from the cells harboring the enzyme or as bait in a two- or three-hybrid system.

USE - The screen is used for identification of modulators which in turn are used in selecting a chemical compound, a drug candidate in drug development (claimed). The compound is utilized for preparing a medicinal product (claimed). Modulators are further used for developing a medicinal product by serving as an interaction probe for identification of putative drug candidates in drug discovery phase (claimed) and thus antibiotic and antifungal agents are identified. Modulators are also used for identifying biomolecules which can be used for improving an industrial fermentation process.

DESCRIPTION OF DRAWING(S) - The diagram shows a schematic representation of pCMVbipep/CI-2A with the functional cis-elements found in pCMVbipep indicated.

Dwg.1/7

L210 ANSWER 17 OF 67 USPATFULL

ACCESSION NUMBER: 1999:155509 USPATFULL

TITLE: Kallikrein-inhibiting "Kunitz Domain" proteins and

analogues thereof

INVENTOR(S): Markland, Willaim, Milford, MA, United States

Ladner, Robert Charles, Ijamsville, MD, United States

PATENT ASSIGNEE(S): Dyax Corp., Cambridge, MA, United States (U.S.

corporation)

1996, now patented, Pat. No. US 5795685 which is a continuation-in-part of Ser. No. US 1994-208264, filed on 10 Mar 1994 which is a continuation-in-part of Ser. No. US 1994-179964, filed on 11 Jan 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Degen, Nancy

LEGAL REPRESENTATIVE: Yankwich, Leon R., Zwicker, Kenneth P.

NUMBER OF CLAIMS: 7 EXEMPLARY CLAIM: 1 LINE COUNT:

2594

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Proteins are disclosed that are homologous to bovine pancreatic trypsin inhibitor (BPTI) Kunitz domains,

and especially proteins that are homologous to lipoprotein-associated coagulation inhibitor (LACI) Kunitz domains,

which inhibit one or more plasma and/or tissue kallikreins, and uses of such proteins in therapeutic and diagnostic methods also are disclosed. In particular, Kunitz domains derived from Kunitz domains of human origin and especially to the first Kunitz domain of LACI

are disclosed.

L210 ANSWER 18 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

2000-072182 [06] WPIDS

DOC. NO. CPI:

C2000-020551

TITLE:

New recombinant nucleic acid, with reduced GC content, encoding the serine protease ASP05, used for treating disorders involving insulin-like growth factor, e.g.

cancer.

DERWENT CLASS:

B04 C03 D16

INVENTOR(S): PATENT ASSIGNEE(S):

HOU, J; SMEEKENS, S P (AXYS-N) AXYS PHARM INC

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO	KIND DATE	WEEK	LA PG
		<i></i>	

A2 19991104 (200006)* EN 70 WO 9955885

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

A 19991116 (200015) AU 9936694

A2 20010207 (200109) EN EP 1073755

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

KR 2001043127 A 20010525 (200168)

APPLICATION DETAILS:

PATENT NO K	CIND	APPLICATION	DATE
WO 9955885	A2 A	WO 1999-US9224 AU 1999-36694	19990428 19990428
EP 1073755	A2	EP 1999-918882 WO 1999-US9224	19990428 19990428
KR 2001043127	7 A	WO 1999-US9224 KR 2000-712020	19990428 20001028

FILING DETAILS:

PATENT NO	KIND	PATENT NO
		WO 000000
AU 9936694	A Based on	WO 9955885 WO 9955885

PRIORITY APPLN. INFO: US 1999-300621 19990427; US 1998-83321P 19980428

AB

WO 9955885 A UPAB: 20011113

NOVELTY - Recombinant nucleic acid (I) has at least a 10% reduction in GC content compared with the sequence of wild-type nucleic acid (Ia) encoding serine protease ASP05.

DETAILED DESCRIPTION - (I) hybridizes, under highly stringent conditions, to nucleotides (nt) 481-1113 of a 1443 bp sequence (S1) (given in the specification), or its complement, and has at least a 10% reduction in GC content compared with the sequence of wild-type nucleic acid (Ia) encoding serine protease ASP05.

INDEPENDENT CLAIMS are also included for the following:

- (a) recombinant nucleic acid encoding amino acids (aa) 30-104 of a 480 aa sequence (S2) (given in the specification);
 - (b) vector containing (I);
 - (c) host cell containing (I) or this vector;
- (d) recombinant production of ASP05 protein (II) by culturing these cells;
 - (e) enzymatically active (II) containing aa 161-371 or 1-480 of (S2);
 - (f) any (II) encoded by (I);
- (g) chimeric molecule (IIa) containing the catalytic domain of ASP05 fused to a heterologous sequence;
 - (h) antibodies (Ab) specific for (II);
- (i) selective cleavage of insulin-like growth factor (IGF) binding protein (IGFBP) by treatment with (IIa) containing aa 161-371 of (S2);
- (j) screening for agents (A) that modulate activity of (II), or any serine protease that can cleave IGFBP selectively;
- (k) modulating cleavage of IGF-BP by administering an exogenous modulator of ASP05; and
- (1) diagnosing an IGF-related condition by detecting abnormal activity of ASP05, relative to a control.

ACTIVITY - Anticancer; antiproliferative; anti-angiogenic.

MECHANISM OF ACTION - ASP05 specifically cleaves IGFBP.

- USE (I) is used to produce recombinant ASP05 proteins (II), particularly in enzymatically active form or fragments, and these are used for selective cleavage of insulin-like growth factor binding protein (IGFBP). (II) can also be used:
 - (1) to raise or purify specific antibodies (Ab);
- (2) to identify modulators (A) of ASP05 (or other serine proteases with similar activity).
- (A), e.g. antisense sequences, antibodies or peptides, are used to reduce or eliminate biological activity of ASP05 proteins, particularly therapeutically, e.g. in cases of cancer; other cell proliferation conditions (restenosis, angiogenesis, neovascularization of the eye etc.); bone metabolic diseases (osteoporosis or osteoarthritis) and diseases of muscle, brain, ovary, uterus and placenta, in human or veterinary medicine. Ab are used therapeutically or for purification of recombinant (II). Determining abnormal levels of ASP05 in tissues is indicative of (risk of) an IGF-related disorder.

ADVANTAGE - (I) is easier to express in transformed cells than the wild-type ASP05 sequence, which has a GC-rich N-terminus. Dwg.0/8

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L210 ANSWER 19 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-371118 [31] WPIDS

CROSS REFERENCE: 1999-229499 [19]; 1999-229532 [19]; 1999-302739 [24]; 1999-326705 [25]; 1999-337420 [25]; 1999-347718 [29]; 1999-404743 [29]; 1999-430385 [35]; 1999-551358 [46]; 1999-580306 [47]; 1999-620728 [53]; 2000-038358 [03]; 2000-062031 [04]; 2000-072883 [05]; 2000-116314 [09]; 2000-237871 [20]; 2000-271386 [23]; 2000-271431 [23];
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2000-271434 [23]; 2000-271435 [23]; 2000-292842 [24];
                      2000-317943 [27]; 2000-412154 [35]; 2000-412324 [35];
                      2000-412325 [35]; 2000-431586 [37]; 2000-442668 [38];
                      2000-452188 [38]; 2000-572269 [52]; 2000-572270 [52];
                      2000-572271 [52]; 2000-587437 [52]; 2000-594320 [52];
                      2000-594321 [52]; 2000-611443 [52]; 2000-611444 [52];
                      2000-628263 [55]; 2000-638138 [52]; 2000-638201 [53];
                      2000-679484 [59]; 2001-016509 [02]; 2001-025022 [66];
                      2001-025251 [02]; 2001-025253 [02]; 2001-032160 [02];
                      2001-050025 [04]; 2001-050091 [05]; 2001-070561 [59];
                      2001-071075 [04]; 2001-071078 [04]; 2001-071395 [06];
                      2001-081051 [09]; 2001-090793 [52]; 2001-091968 [10];
                      2001-103149 [11]; 2001-183260 [18]; 2001-226690 [20];
                      2001-226823 [23]; 2001-235264 [23]; 2001-381383 [39];
                      2001-381384 [39]; 2001-408281 [39]; 2001-451708 [43];
                      2001-541567 [53]; 2001-602746 [62]; 2001-625876 [60];
                      2002-075461 [03]; 2002-090516 [09]; 2002-130120 [14];
                      2002-130151 [22]; 2002-130882 [09]; 2002-171999 [22];
                      2002-172001 [22]; 2002-205567 [49]; 2002-256031 [46];
                      2002-280917 [30]; 2002-280928 [30]; 2002-280940 [30];
                      2002-292065 [30]
DOC. NO. CPI:
                      C1999-109584
                     Nucleic acids encoding PRO secreted and transmembrane
TITLE:
                      proteins.
DERWENT CLASS:
                      B04 D16 S03
                     BAKER, K P; CHEN, J; GODDARD, A; GURNEY, A L; WOOD, W I;
INVENTOR(S):
                      YUAN, J; GURNEY, A
                      (GETH) GENENTECH INC; (LUCE) LUCENT TECHNOLOGIES INC;
PATENT ASSIGNEE(S):
                      (BAKE-I) BAKER K P; (CHEN-I) CHEN J; (GODD-I) GODDARD A;
                      (GURN-I) GURNEY A L; (WOOD-I) WOOD W I; (YUAN-I) YUAN J
COUNTRY COUNT:
                      85
PATENT INFORMATION:
                             WEEK
                                        LA
                                              PG
     PATENT NO KIND DATE
     WO 9928462 A2 19990610 (199931)* EN 123
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
            GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
            MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA
            UG US UZ VN YU ZW
     AU 9916029
                A 19990616 (199945)
     ZA 9811071 A 19991027 (199951)
                                             123
     AU 9922122 A 19990726 (199952)
     JP 11355431 A 19991224 (200011)
                                              11
                  A 20000105 (200021)
     CN 1240321 A 20000105 (200021)
EP 1037979 A2 20000927 (200048) EN
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI
                  B 20010726 (200149)
     AU 736506
     KR 2001032719 A 20010425 (200164)
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APPLICATION DETAILS:

RO SE SI

MX 2000005354 A1 20010401 (200171) JP 2002505850 W 20020226 (200219)

A2 20020327 (200229) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

202

R. Mitra; 09/667,380

PAT	ENT NO K	IND			API	PLICATION	DATE
WO.	9928462	A2	- 		WO	1998-US25108	19981201
AU	9916029	Α			AU	1999-16029	19981201
	9811071	Α			ZA	1998-11071	19981203
AU	9922122	Α			ΑU	1999-22122	19990105
JР	11355431	Α			JP	1999-130879	19990512
CN	1240321	Α			CN	1999-106448	19990511
EP	1037979	A2			EP	1998-960440	19981201
					WO	1998-US25108	19981201
ΑU	736506	В			ΑU	1999-16029	19981201
KR	2001032719	Α			WO	1998-US25108	19981201
					KR	2000-706008	20000602
MX	2000005354	A1			MX	2000-5354	20000531
JР	2002505850	W			WO	1998-US25108	19981201
					JP	2000-523338	19981201
EP	1191101	A2	Div	ex	EP	1998-960440	19981201
					EP	2001-126188	19981201

FILING DETAILS:

PATENT NO	KIND		PAT	CENT NO	
AU 9916029	A Base	d on		9928462	
AU 9922122	A Base	d on	WO	9935170	
EP 1037979	A2 Base	d on	WO	9928462	
AU 736506	B Prev	ious Publ.	ΑU	9916029	
	Base	d on	. WO	9928462	
JP 20025058	50 W Base	d on	WO	9928462	
EP 1191101	A2 Div	ex	\mathbf{EP}	1037979	

PRIORITY APPLN. INFO: US 1998-75945P 19980225; US 1997-67411P 19971203; US 1997-69278P 19971211; US 1997-69334P 19971211; US 1997-69335P 19971211; US 1997-69425P 19971212; US 1997-69694P 19971216; US 1997-69696P 19971216; US 1997-69702P 19971216; US 1997-69870P 19971217; US 1997-69873P 19971217; US 1997-68017P 19971218; US 1998-70440P 19980105; US 1998-74086P 19980209; US 1998-74092P 19980209; US 19980429; US 1998-86414P 1998-83500P 19980522; US 1998-88742P 19980610; US 1998-107783P 19981110; US 1998-109304P 19981120; US 1998-75945 19980512

AB WO 9928462 A UPAB: 20020524

NOVELTY - Nucleic acids encoding PRO secreted and transmembrane proteins used therapeutically are new.

DETAILED DESCRIPTION - A novel nucleic acid is at least 80% identical to a sequence encoding a PRO polypeptide having a 379, 954, 737, 433, 446, 422, 300, 243, 455, 694, 440, 598, 250, 281, 431 or 235 amino acid sequence (all given in the specification).

INDEPENDENT CLAIMS are also included for the following:

- (1) a vector comprising a nucleic acid as above;
- (2) a host cell comprising a vector as in (1);
- (3) production of a PRO polypeptide as above; a PRO polypeptide at least 80% identical to a sequence as described above;
- (4) a chimeric molecule comprising a PRO polypeptide as above fused to a heterologous amino acid sequence; and
 - (5) an antibody which specifically binds to a PRO polypeptide as

above.

ACTIVITY - Cytostatic; Anti-inflammatory; Anti-proliferative; Immunosuppressive.

MECHANISM OF ACTION - None given.

USE - The proteins and polynucleotides can be used in therapy, identification of homologues, raising antibodies and design of probes and primers. They can be used in a range of diseases related to proteins that they have homology with, e.g. a PRO protein having homology to complement proteins may be used in inflammatory responses.

ADVANTAGE - None given.

Dwg.0/39

L210 ANSWER 20 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER:

1999335882 EMBASE

TITLE:

Inactivation of proprotein convertase, PACE4, by

.alpha.1-antitrypsin portland (.alpha.1-PDX), a blocker of proteolytic activation of bone morphogenetic protein during

embryogenesis: Evidence that PACE4 is able to form an

SDS-stable acyl intermediate with .alpha.1-PDX.

AUTHOR:

Tsuji A.; Hashimoto E.; Ikoma T.; Taniguchi T.; Mori K.;

Nagahama M.; Matsuda Y.

CORPORATE SOURCE:

Y. Matsuda, Dept. Biological Science Technology, Faculty of

Engineering, The University of Tokushima, 2-1 Minamijosanjima, Tokushima 770 8506, Japan.

matsuda@bio.tokushima-u.ac.jp

SOURCE:

Journal of Biochemistry, (1999) 126/3 (591-603).

Refs: 51

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY:

Japan

Journal; Article DOCUMENT TYPE:

Developmental Biology and Teratology FILE SEGMENT: 021

Clinical Biochemistry 029

LANGUAGE:

English English

SUMMARY LANGUAGE: PACE4 (SPC4), a member of the subtilisin-like proprotein convertase (SPC) family of proteases that cleave at paired basic amino acids, exhibits a dynamic expression pattern during embryogenesis and colocalizes with bone morphogenetic proteins (BMPs). Recently Cui et al. reported that the ectopic expression of .alpha.1-antitrypsin variant Portland (.alpha.1-PDX), an engineered serpin that contains the minimal SPC

consensus motif in its reactive loop, blocks the proteolytic activation of BMP4, leading to abnormal embryogenic development TGF.beta.-related factors such as BMPs are synthesized as inactive precursors and activated by limited proteolysis at multibasic amino acids. Therefore, an .alpha.1-PDX-inhibitable protease is thought to participate in BMP activation. However, conflicting properties, including sensitivity to .alpha.1-PDX, have been reported for PACE4. In this study, we examined whether .alpha.1-PDX is responsible for the inhibition of PACE4 by measuring the protease/inhibitor complex directly. Here we show that .alpha.1-PDX has the ability to form an SDS-stable acyl-intermediate (180 kDa) with PACE4 in vivo and in vitro. Further, we characterized the PACE4 secreted into the culture medium from Cos-1 cells by a specific immunological assay. An .alpha.1-PDX-insensitive and decanoyl-RVKRchloromethylketone-sensitive 60-kDa protease(s) is greatly activated in conditioned medium by PACE4 overexpression, suggesting that the activation of an unknown protease(s) other than PACE4 is the cause of the variation in the properties of PACE4. PACE4 is a Ca2+-dependent protease with an

optimal Ca2+ requirement of 2 mM, and shows its highest activity at weakly basic pH. PACE4 activity is completely inhibited by EDTA and EGTA, but not by leupeptin. These results show that PACE4 activity can be inhibited by (.alpha.1-PDX as well as furin (SPC1) and suggest that the inhibition of PACE4-mediated activation of factors such as BMPs by .alpha.1-PDX causes abnormal embryogenic development.

L210 ANSWER 21 OF 67 USPATFULL

ACCESSION NUMBER: 1998:98889 USPATFULL

TITLE:

Kallikrein-inhibiting "kunitz domain" proteins and

analogues thereof

INVENTOR(S):

Markland, Willaim, Milford, MA, United States

Ladner, Robert Charles, Ijamsville, MD, United States

PATENT ASSIGNEE(S):

Dyax Corp., Cambridge, MA, United States (U.S.

corporation)

	NUMBER	KIND DATE	
PATENT INFORMATION:	US 5795865	19980818	
	WO 9521601	19950817	
APPLICATION INFO.:	US 1996-676125	19960925	(8)
111111111111111111111111111111111111111	WO 1995-US299	19950111	
·		19960925	PCT 371 date
		19960925	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-208264, filed

on 10 Mar 1994, now abandoned And a

continuation-in-part of Ser. No. US 1994-179964, filed

on 11 Jan 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Degen, Nancy

LEGAL REPRESENTATIVE: Yankwich, Leon R., Cooper, Iver P.

NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 2161

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Proteins are disclosed that are homologous to bovine pancreatic trypsin inhibitor (BPTI) Kunitz domains, and especially proteins that are homologous to lipoprotein-associated coagulation inhibitor (LACI) Kunitz domains, which inhibit one or more plasma and/or tissue kallikreins, and uses of such proteins in therapeutic and diagnostic methods also are disclosed. In particular, Kunitz domains derived from Kunitz domains of human origin and especially to the first Kunitz domain of LACI are disclosed.

L210 ANSWER 22 OF 67 USPATFULL

ACCESSION NUMBER: 199

1998:95406 USPATFULL

TITLE:

Isolated DNA encoding novel protease inhibitory

polypeptide

INVENTOR(S):

Morishita, Hideaki, Tokyo, Japan Kanamori, Toshinori, Tokyo, Japan Nobuhara, Masahiro, Tokyo, Japan

PATENT ASSIGNEE(S):

Mochida Pharmaceutical Co., Ltd., Tokyo, Japan

(non-U.S. corporation)

RELATED APPLN. INFO.:

Division of Ser. No. US 1991-791213, filed on 13 Nov

1991, now patented, Pat. No. US 5409895

NUMBER DATE _____

JP 1990-306745 19901113 PRIORITY INFORMATION:

Utility DOCUMENT TYPE: Granted FILE SEGMENT:

Wax, Robert A. PRIMARY EXAMINER: ASSISTANT EXAMINER: Grimes, Eric

LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, LLP

NUMBER OF CLAIMS: 29 EXEMPLARY CLAIM:

50 Drawing Figure(s); 34 Drawing Page(s) NUMBER OF DRAWINGS:

5022 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a novel polypeptide which comprises an amino acid sequence that constitutes a portion of urinary trypsin inhibitor (UTI) and which has no antigenicity against human and high activity to inhibit various proteases, as well as other novel polypeptides having excellent activities to inhibit various proteases obtained by mutation of the former novel polypeptide. This invention also provides novel enzyme inhibition processes, drug compositions and treating methods making use of the novel polypeptide, DNA fragments containing nucleotide sequences which encode the novel polypeptides, vectors containing the DNA fragments and transformants transformed with the DNA fragments or the vectors, as well as processes for the production of the novel polypeptides.

L210 ANSWER 23 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1999-070328 [06] WPIDS

DOC. NO. CPI:

C1999-020862

TITLE:

Production of heterologous polypeptide containing many disulphide bonds in bacteria - that also express a disulphide isomerase to ensure proper folding and increased yield of biologically active product, e.g. tissue plasminogen activator or pancreatic trypsin

inhibitor.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BESSETTE, P; GEORGIOU, G; QIU, J; SWARTZ, J R; OIU, J;

SWARTZ, J

PATENT ASSIGNEE(S):

(TEXA) UNIV TEXAS SYSTEM; (GETH) GENENTECH INC

COUNTRY COUNT:

83

PATENT INFORMATION:

WEEK KIND DATE PATENT NO _____

WO 9856930 A2 19981217 (199906)* EN 97

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU I'D IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG

US UZ VN YU ZW

A 19981230 (199920) AU 9881404 A2 20000524 (200030) EN EP 1002111

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

US 6083715 A 20000704 (200036) JP 2002504826 W 20020212 (200215) AU 743030 B 20020117 (200219) 106

APPLICATION DETAILS:

PATENT NO K	IND	APPLICATION	DATE
WO 9856930	A2	WO 1998-US12004	19980609
AU 9881404 EP 1002111	A A2	AU 1998-81404 EP 1998-931228	19980609 19980609
US 6083715	A	WO 1998-US12004 US 1997-871483	19980609 19970609
JP 2002504826	M	WO 1998-US12004 JP 1999-503144	19980609
AU 743030	В	AU 1998-81404	19980609 19980609

FILING DETAILS:

PATENT NO K	IND	PATENT NO
AU 9881404	A Based on	WO 9856930
EP 1002111	A2 Based on	WO 9856930
JP 2002504826	W Based on	WO 9856930
AU 743030	B Previous Publ.	AU 9881404
	Based on	WO 9856930

PRIORITY APPLN. INFO: US 1997-871483 19970609 AB WO 9856930 A UPAB: 19990210

Production of a heterologous polypeptide (I) comprises culturing bacteria that contain (i) nucleic acid (NA1) encoding a disulphide isomerase (DsbG) protein (II); (ii) nucleic acid (NA2) encoding (I); (iii) signal sequence for secretion of both (I) and (II) and (iv) separate inducible promoters for NA1 and 2. The cells are cultured such that (II) is expressed before (I), and such that (a) both (I) and (II) are secreted into the periplasm or (b) (I) is secreted into the culture medium. (I) is then recovered from periplasm or medium. Also new are (1) method for producing biologically active, soluble eukaryotic polypeptide (Ia) with four or more disulphide bridges by expressing, in bacteria, a DNA encoding DsbC or DsbG linked to a signal sequence, and a second DNA encoding (Ia), also linked to a signal sequence; (2) bacterial expression system that expresses DsbC or G protein and recombinant eukaryotic polypeptide (Ib) with four or more disulphide bonds; (3) recombinant vector containing first transcription unit encoding E. coli DsbC or G linked to a signal sequence and second such unit expressing mammalian tissue plasminogen activator (tPA) or pancreatic trypsin inhibitor (PTI); (4) active tPA or PTI linked to a bacterial export signal peptide; (5) soluble, recombinant human tPA, protein or peptide, isolated from the periplasm of a cell in biologically active form; (6) E. coli ATCC 98380; (7) polypeptide (III) containing at least 15 contiguous amino acids (aa) from a 268 aa sequence reproduced (the DsbG protein) and able to catalyse disulphide bond formation; (8) polynucleotide (IV) encoding a bacterial disulphide isomerase containing at least 40 contiguous nucleotides (nt) from a 46 nt sequence reproduced (or with a sequence that hybridises with this under stringent conditions); (9) production of recombinant tPA in bacteria by co-expression with a cysteine oxidoreductase that facilitates production of active tPA.

USE - The methods are particularly used to produce insulin-like growth factor (IGF), or its receptor, tPA and PTI, but more generally any (I) that contains numerous disulphide bonds (e.g. antibody fragments, enzymes, lymphokines, neurotrophins and many others disclosed).

ADVANTAGE - Co-expression with DsbG or C results in active, correctly folded (I), even where this contains many disulphide bridges. (I) are produced in much increased yield, without requiring addition of

glutathione or co-expression of the heat-shock transcription factor RpoH. Production of (I) in secreted form facilitates purification, i.e. no need to solubilise and refold material present in inclusion bodies, and results in a product of higher activity. Dwg.1B/11

L210 ANSWER 24 OF 67 MEDLINE

ACCESSION NUMBER: 1998352217 MEDLINE

DOCUMENT NUMBER: 98352217 PubMed ID: 9685498

TITLE: Divergent expression of alphal-protease inhibitor genes in

mouse and human.

AUTHOR: Tardiff J; Krauter K S

CORPORATE SOURCE: Department of Molecular, Cellular and Developmental

Biology, University of Colorado at Boulder, Campus Box 347,

Boulder, CO 80309, USA.

CONTRACT NUMBER: CA13330 (NCI)

CA39553 (NCI)

SOURCE: NUCLEIC ACIDS RESEARCH, (1998 Aug 15) 26 (16) 3794-9.

Journal code: O8L; 0411011. ISSN: 0305-1048.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-M75716; GENBANK-M75717; GENBANK-M75718;

GENBANK-M75720; GENBANK-M75721

ENTRY MONTH: 199809

ENTRY DATE: Entered STN: 19981006

Last Updated on STN: 20000303 Entered Medline: 19980922

The alpha1-protease inhibitor proteins of laboratory mice are homologous AB in sequence and function to human alphal-antitrypsin and are encoded by a highly conserved multigene family comprised of five members. In humans, the inhibitor is expressed in liver and in macrophages and decreased expression or inhibitory activity is associated with a deficiency syndrome which can result in emphysema and liver disease in affected individuals. It has been proposed that macrophage expression may be an important component of the function of human alphal-antitrypsin. Clearly, it is desirable to develop a mouse model of this deficiency syndrome, however, efforts to do this have been largely unsuccessful. In this paper, we report that aside from the issues of potentially redundant gene function, the mouse may not be a suitable animal for such studies, because there is no significant expression of murine alphal-protease inhibitor in the macrophages of mice. This difference between the species appears to result from an absence of a functional macrophage-specific promoter in mice.

L210 ANSWER 25 OF 67 MEDLINE

ACCESSION NUMBER: 97277372 MEDLINE

DOCUMENT NUMBER: 97277372 PubMed ID: 9115294

TITLE: Identification and cloning of human placental bikunin, a

novel serine protease inhibitor containing two Kunitz

domains.

AUTHOR: Marlor C W; Delaria K A; Davis G; Muller D K; Greve J M;

Tamburini P P

CORPORATE SOURCE: Institute of Bone and Joint Disease and Cancer, Bayer

Corporation, West Haven, Connecticut 06516, USA.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 May 2) 272 (18)

12202-8.

Journal code: HIV; 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

Searched by Thom Larson, STIC, 308-7309

LANGUAGE:

English

FILE SEGMENT: OTHER SOURCE: Priority Journals GENBANK-U78095

ENTRY MONTH:

199706

ENTRY DATE:

Entered STN: 19970612

Last Updated on STN: 19970612

Entered Medline: 19970602

Interrogation of the public expressed sequence tag (EST) data base with AB the sequence of preproaprotinin identified ESTs encoding two potential new members of the Kunitz family of serine protease inhibitors. Through reiterative interrogation, an EST contig was obtained, the consensus sequence from which encoded both of the novel Kunitz domains in a single open reading frame. This consensus sequence was used to direct the isolation of a full-length cDNA clone from a placental library. The resulting cDNA sequence predicted a 252-residue protein containing a putative NH2-terminal signal peptide followed sequentially by each of the two Kunitz domains within a 170-residue ectodomain, a putative transmembrane domain, and a 31-residue hydrophilic COOH terminus. The gene for this putative novel protein was mapped by use of a radiation hybrid panel to chromosome 19q13, and Northern analysis showed that the corresponding mRNA was expressed at high levels in human placenta and pancreas and at lower levels in brain, lung, and kidney. An endogenous soluble form of this protein, which was designated as placental bikunin, was highly purified from human placenta by sequential kallikrein-Sepharose affinity, gel filtration, and C18 reverse-phase chromatography. The natural protein exhibited the same NH2 terminus as predicted from the cloned cDNA and inhibited trypsin, plasma kallikrein, and plasmin with IC50 values in the nanomolar range.

L210 ANSWER 26 OF 67 USPATFULL

ACCESSION NUMBER:

INVENTOR (S):

96:27176 USPATFULL

TITLE:

Agent for treating or preventing AIDS using

human urine trypsin inhibitor
Hattori, Toshio, Kumamoto, Japan
Takatsuki, Kiyoshi, Kumamoto, Japan

Yuki, Yoshikazu, Kobe, Japan

PATENT ASSIGNEE(S):

JCR Pharmaceuticals Co., Ltd., Hyogo, Japan (non-U.S.

corporation)

NUMBER KIND DATE
-----US 5504065 19960402
US 1994-261746 19940617 (8)

PATENT INFORMATION:
APPLICATION INFO.:
RELATED APPLN. INFO.:

US 1994-261746 19940617 (8)
Continuation of Ser. No. US 1993-158819, filed on 26
Nov 1993, now abandoned which is a continuation of Ser.
No. US 1992-960199, filed on 9 Oct 1992, now abandoned which is a continuation of Ser. No. US 1992-831080, filed on 5 Feb 1992, now abandoned which is a

continuation of Ser. No. US 1989-436830, filed on 15

Nov 1989, now abandoned

NUMBER DATE

PRIORITY INFORMATION: DOCUMENT TYPE:

JP 1988-302058

19881128

FILE SEGMENT: PRIMARY EXAMINER: Utility Granted

Schain, Howard E.

LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: EXEMPLARY CLAIM:

LEGAL REPRESENTATIVE: Burgess, Ryan and Wayne

. 2 1 NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 273

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Human urine trypsin inhibitor is provided as an agent for treating acquired immunodeficiency syndrome (AIDS), preventing the infection with AIDS or preventing the onset of AIDS after such infection. It can be administered intravenously for the treatment and externally for the prevention.

L210 ANSWER 27 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96187771 EMBASE

DOCUMENT NUMBER: 1996187771

TITLE: Isolation and characterization of the human

inter-.alpha.-trypsin inhibitor family heavy chain-related

protein (IHRP) gene (ITIHL1).

AUTHOR: Saguchi K.-I.; Tobe T.; Hashimoto K.; Nagasaki Y.; Oda E.;

Nakano Y.; Miura N.-H.; Tomita M.

CORPORATE SOURCE: Dept. of Physiological Chemistry, School of Pharmaceutical

Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku,

Tokyo 242, Japan

SOURCE: Journal of Biochemistry, (1996) 119/5 (898-905).

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English
SUMMARY LANGUAGE: English

Inter-.alpha.-trypsin inhibitor (ITI) family heavy chain-related protein (IHRP) is a novel human glycoprotein that shows significant homology in amino acid sequence to proteins of the ITI family heavy chains from human plasma. Three overlapping clones that encode the human inter-.alpha.-trypsin inhibitor family heavy chain-related protein (IHRP) gene (ITIHL1) were isolated and characterized. The IHRP gene spans 15 kb and is composed of 24 exons from 27 to 207 bp in size with consensus splice sites. The gene codes for the precursor of IHRP, which is similar to inter-a-trypsin inhibitor (ITI) family heavy chains. Two major transcription initiation sites were identified in the 5'-flanking region. They contain putative promoter elements, but no typical TATA box. Some exons of this gene showed significant similarities to those of the ITI-H1 gene in nucleotide length and in intron phasing. The tissue-specific transcription of this gene may be due to the presence of binding sites for the hepatocyte nuclear factors LF-A1, HNF-5, NP-IL6, and C/EBP. This gene was found to be localized very close to another unknown gene related to EST (GenBank accession: R54643, R50663, R50563, H27139, and R54913).

L210 ANSWER 28 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96115912 EMBASE

DOCUMENT NUMBER: 1996115912

TITLE: CDNA cloning and primary structure of tryptase from bovine

mast cells, and evidence for the expression of bovine pancreatic typsin inhibitor mRNA in the same cells.

AUTHOR: Pallaoro M.; Gambacurta A.; Fiorucci l.; Mignogna G.; Barra

D.; Ascoli F.

CORPORATE SOURCE: Dpt. Medic. Speriment./Sci. Biochim., Universita Tor

Vergata, Via di Tor Vergata 135,I-00133 Roma, Italy

SOURCE: European Journal of Biochemistry, (1996) 237/1 (100-105).

ISSN: 0014-2956 CODEN: EJBCAI

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT:

029 Clinical Biochemistry

LANGUAGE:

English

SUMMARY LANGUAGE:

English

A partial cDNA encoding bovine tryptase, an oligomeric serine proteinase previously isolated from bovine mast cells, was obtained by reverse transcription/polymerase chain reaction of mast cell mRNA, using combinations of primers designed on the basis of information obtained from partial sequencing of the purified protein. The complete amino acid sequence of bovine tryptase (245 residues) was deduced from a 711-bp nucleotide sequence and from Edman degradation of the protein. Bovine tryptase primary structure has an identity of about 75 % with tryptases from other species-and includes all the essential residues of the active-site regions; sequence data in the region of the putative substrate binding pocket suggest a rearrangement capable of maintaining the specificity of trypsin-like proteinases. From the same mast cell mRNA, cDNA encoding bovine trypsin protease inhibitor (BPTI) was obtained and amplified with specific primers, confirming the synthesis of BPTI in these cells. Results are consistent with previous. data on the presence of BPTI

L210 ANSWER 29 OF 67 USPATFULL

their interaction in vitro.

ACCESSION NUMBER:

95:36370 USPATFULL

TITLE:

Protease inhibitory polypeptides derived from urinary

trypsin inhibitor and compositions thereof

INVENTOR(S):

Morishita, Hideaki, Tokyo, Japan Kanamori, Toshinori, Tokyo, Japan Nobuhara, Masahiro, Tokyo, Japan

and bovine tryptase in the same granules of bovine mast cells and with

PATENT ASSIGNEE(S):

Mochida Pharmaceutical Co., Ltd., Tokyo, Japan

(non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION:

US 5409895 US 1991-791213 19950425 19911113 (7)

APPLICATION INFO.:

NUMBER DATE ______

PRIORITY INFORMATION:

JP 1990-306745 19901113

DOCUMENT TYPE: Utility

Granted

FILE SEGMENT:

PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Grimes, Eric

LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

50 Drawing Figure(s); 34 Drawing Page(s)

LINE COUNT:

3694

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a novel polypeptide which comprises an amino acid sequence that constitutes a portion of urinary

trypsin inhibitor (UTI) and which has no antigenicity against

human and high activity to inhibit various

proteases, as well as other novel polypeptides having excellent

activities to inhibit various proteases obtained by

mutation of the former novel polypeptide. This invention also provides novel enzyme inhibition processes, drug compositions and treating methods making use of the novel polypeptide, DNA fragments containing nucleotide sequences which encode the novel polypeptides,

vectors containing the DNA fragments and transformants transformed with

the DNA fragments or the vectors, as well as processes for the production of the novel polypeptides.

L210 ANSWER 30 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

95078767 EMBASE ACCESSION NUMBER:

1995078767 DOCUMENT NUMBER:

The three heavy-chain precursors for the TITLE:

inter-.alpha.-inhibitor family in mouse: New members of the

multicopper oxidase protein group with differential

transcription in liver and brain.

Chan P.; Risler J.-L.; Raguenez G.; Salier J.-P. **AUTHOR:**

INSERM U-78, BP 73,76233 Boisguillaume Cedex, France CORPORATE SOURCE:

Biochemical Journal, (1995) 306/2 (505-512). SOURCE:

ISSN: 0264-6021 CODEN: BIJOAK

United Kingdom COUNTRY: Journal; Article DOCUMENT TYPE:

Human Genetics 022 FILE SEGMENT:

Clinical Biochemistry 029

English LANGUAGE: English SUMMARY LANGUAGE:

The inter-.alpha.-inhibitor (I.alpha.I) family is comprised of the plasma protease inhibitors I.alpha.I, inter-.alpha.-like inhibitor (I.alpha.LI), pre-.alpha.-inhibitor (P.alpha.I) and bikunin. I.alpha.I, I.alpha.LI and P.alpha.I are distinct assemblies of bikunin with one of three heavy (H) chains designated H1, H2 and H3. These H chains and bikunin are respectively encoded by a set of three H genes and an .alpha.1microglobulin/bikunin precursor (AMBP) gene. All four gene products undergo maturation steps from precursor polypeptides. The full-length cDNAs for the H1-, H2- and H3-chain precursors were cloned from a mouse liver cDNA library and sequenced. Extensive searches of amino acid sequence similarities to other proteins in databanks revealed (i) a highly significant similarity of the C-terminal sequence in the three H-chain precursors to the multicopper-binding domain in the group of multicopper oxidase proteins and (ii) the presence of von Willebrand type-A domains in the mature H chains. Amino acid sequence comparisons between the three mouse H1-, H2- and H3-chain precursors and their human counterparts allowed us to appraise the timing and order of occurrence of the three H-chain genes from a shared ancestor during mammalian evolution. Owing to a multiple alignment of the six mouse and human nucleotide sequences for these H-chain precursors, a reverse transcriptase PCR assay with degenerate oligonucleotides was designed, allowing us to (i) present evidence that no mRNAs for further H genes exist in mouse liver and (ii) demonstrate a previously undescribed transcription of the H2- and H3-chain mRNAs in mouse brain, which contrasts with the expression of all four, H1, H2, H3 and AMBP, mRNAs in liver.

L210 ANSWER 31 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

95282561 EMBASE ACCESSION NUMBER:

DOCUMENT NUMBER: 1995282561

Pancreatic secretory trypsin inhibitor gene is highly TITLE:

expressed in the liver of adult-onset type II

citrullinemia.

Kobayashi K.; Nakata M.; Terazono H.; Shinsato T.; Saheki AUTHOR:

Department of Biochemistry, Faculty of Medicine, Kagoshima CORPORATE SOURCE:

University, Sakuragaoka 8-35-1, Kagoshima 890, Japan

FEBS Letters, (1995) 372/1 (69-73). SOURCE:

ISSN: 0014-5793 CODEN: FEBLAL

Netherlands COUNTRY:

Journal; Article DOCUMENT TYPE:

Human Genetics 022 FILE SEGMENT:

Clinical Biochemistry 029

Gastroenterology 048

English LANGUAGE:

SUMMARY LANGUAGE: English Deficiency of argininosuccinate synthetase (ASS) causes citrullinemia. Type II citrullinemia is found in most patients with adult-onset citrullinemia in Japan, and ASS is deficient specifically in the liver. Previous studies have shown that the decrease of hepatic ASS activity is caused by a decrease in enzyme protein with normal kinetic properties and that there are no apparent abnormalities in the amount, translational activity, and nucleotide sequence of hepatic ASS mRNA. Recent results of homozygosity testing indicate that the primary defect of type II citrullinemia is not within the ASS gene locus. In this present work, to understand the pathogenesis and pathophysiology of type II citrullinemia, we have characterized the alterations of gene expression in the liver of type II patients using the recently developed mRNA differential display method. Some cDNA bands expressed differently in type II citrullinemia patients and control were selected, cloned, and sequenced. Nucleotide sequence analysis and homology searching revealed an interesting clone which has 99% homology with the human pancreatic secretory trypsin inhibitor (hPSTI). Northern blot and RT-PCR analyses showed that the expression of hPSTI mRNA increased significantly in the liver of all type II patients tested. Furthermore, the concentration of hPSTI protein was found to be higher in the liver of type II citrullinemia than in control. These results suggest that hPSTI may be related to the primary defect of type II citrullinemia and may be useful as a diagnostic marker, although the detailed mechanism of the high expression of hPSTI mRNA in type II liver is not yet known.

L210 ANSWER 32 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94235128 EMBASE

1994235128

DOCUMENT NUMBER:

Translational enhancement of H-ferritin mRNA by TITLE: interleukin-1.beta. acts through 5' leader sequences

distinct from the iron responsive element.

Rogers J.T.; Andriotakis J.L.; Lacroix L.; Durmowicz G.P.; **AUTHOR:**

Kasschau K.D.; Bridges K.R.

Division of Hematology-Oncology, Department of Medicine, CORPORATE SOURCE:

Brigham and Women's Hospital, Boston, MA 02115, United

States

Nucleic Acids Research, (1994) 22/13 (2678-2686). SOURCE:

ISSN: 0305-1048 CODEN: NARHAD

United Kingdom COUNTRY: Journal; Article DOCUMENT TYPE:

Human Genetics 022 FILE SEGMENT:

Immunology, Serology and Transplantation 026

Clinical Biochemistry 029

English LANGUAGE: English SUMMARY LANGUAGE:

Interleukin-1.beta. (II-1.beta.), a key cytokine in the acute phase response, elevates hepatic expression of both the heavy (H) and light (L) ferritin subunits without influencing the steady-state levels of either ferritin transcript. Transfection experiments with human hepatoma cells reveal that sequences within the 5' untranslated region (5'UTR) of H-ferritin mRNA confer translational regulation to chimaeric chloramphenicol acetyl transferase (CAT) mRNAs in response to II-1.beta. in the absence of marked changes in CAT mRNA levels. dependent translational enhancement is mediated by a distinct G + C rich RNA sequence within 70 nucleotides (nt) of the start codon. The upstream Iron Responsive Element RNA stemloop does not confer increased expression to CAT mRNA in II-1.beta. stimulated hepatoma transfectants. A 38 nucleotide consensus sequence within the 5'UTRs of the mRNAs encoding the hepatic acute phase proteins .alpha.1-antitrypsin (.alpha.1AT), .alpha.1-acid glycoprotein (AGP) and haptoglobin is similar to sequences in the G+C rich H-ferritin mRNA translational regulatory element. Deletion of three nucleotides from this region of the 61 nt G + C rich element in the H-ferritin mRNA 5' leader eliminates II-1.beta. translational enhancement of the CAT reporter transcripts.

L210 ANSWER 33 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93064647 EMBASE

DOCUMENT NUMBER: 1993064647

TITLE: Organization and sequence of the gene encoding the human

acrosin-trypsin inhibitor (HUSI-II).

AUTHOR: Moritz A.; Grzeschik K.-H.; Wingender E.; Fink E.

CORPORATE SOURCE: Dept. Clin. Chemistry/Clin. Biochem., University of Munich,

Nussbaumstrasse 20, D-8000 Munich 2, Germany

SOURCE: Gene, (1993) 123/2 (277-281).

ISSN: 0378-1119 CODEN: GENED6

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

A complete cDNA encoding the acrosin-trypsin inhibitor, HUSI-II, was used as a probe to isolate genomic clones from a human placenta library. Three clones which cover the entire HUSI-II gene were isolated and characterized. The exon-intron organization of the gene was determined and found to be identical to other known Kazal-type inhibitor encoding genes. The striking similarity in the amino acid sequences which was found previously in HUSI-II and glycoprotein hormone .beta.-subunits, is neither reflected in codon usage nor in the exon-intron arrangement of the genes. A 1.8-kb segment 5' of the gene was sequenced. The analysis of this sequence showed that HUSI-II contains a G+C-rich region upstream from the transcription start point (tsp) which fulfills the criteria for a CpG island. Furthermore, in the first intron, a potential glucocorticoidresponsive element was found as a half-palindrome flanked by two CACCC elements. Determination of the tsp by S1 mapping revealed that HUSI-II has multiple tsp. Genomic Southern hybridization was used to show that HUSI-II is a single-copy gene. The localization of the gene to chromosome 4 was determined by hybridization of a 5' genomic fragment to the DNA of a panel of somatic hybrids between human and rodent cells.

L210 ANSWER 34 OF 67 USPATFULL

ACCESSION NUMBER: 92:49128 USPATFULL

TITLE: Modified human pancreatic secretory

trypsin inhibitor

INVENTOR(S): Yoshida, Nobuo, Nishinomiya, Japan

Kikuchi, Norihisa, Takatsuki, Japan

Shin, Masaru, Kobe, Japan

Teraoka, Hiroshi, Sakai, Japan

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Osaka, Japan (non-U.S.

corporation)

Searched by Thom Larson, STIC, 308-7309

NUMBER DATE _______

JP 1988-181316 19880719 JP 1988-255580 19881011 PRIORITY INFORMATION:

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

PRIMARY EXAMINER: Lacey, David L. ASSISTANT EXAMINER: Ossanna, Nina LEGAL REPRESENTATIVE: Morrison & Foerster

NUMBER OF CLAIMS: 4 1 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 11 Drawing Figure(s); 10 Drawing Page(s)

989 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DNA sequences encoding modified varieties of human PSTI possessing excellent stability in terms of decreased susceptibility to decomposition by proteolytic enzymes such as trypsin, as compared with natural human PSTI, as well as the modified varieties of human PSTI obtained by the expression of the DNA sequences.

L210 ANSWER 35 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1993-402585 [50] WPIDS

DOC. NO. CPI: C1993-179265

TITLE: New strain of hybrid cells Mus musculus L - can be used

for prodn. of monoclonal antibodies to acid-stable

trypsin inhibitor from human

urine.

DERWENT CLASS: B04 D16

MARIO, B; OGLOBLINA, O G; RALPH, B INVENTOR(S): PATENT ASSIGNEE(S): (AMCA-R) A MED CARDIOLOGY RES CENTRE

COUNTRY COUNT: 1 PATENT INFORMATION:

> PATENT NO KIND DATE WEEK LA PG _____ SU 1778183 A1 19921130 (199350)*

APPLICATION DETAILS:

APPLICATION PATENT NO KIND DATE SU 1778183 A1 SU 1990-4879754 19901102

PRIORITY APPLN. INFO: SU 1990-4879754 19901102

SU 1778183 A UPAB: 19940203

New strain of hybrid cultivable cells Mus musculus L, producing monoclonal antibodies to trypsin-binding part of acid-stable trypsin inhibitor from human urine, is stored in National Collection of cell cultures under No. VSKK/P/505D.

New strain is obtd. by hybridisation of splenocytes of mouse Balb/c with mouse myeloma cells P301. Secretion of monoclonal antibodies on the 4th day of culturing in vitro reaches 10-25 micro-q/ml and in ascitic liq. 5-10 mg/ml. Monoclonal antibodies refer to Ig61. Stable prodn. of antibodies continues for 40 passages in vitro and in

USE/ADVANTAGE - New strain can be used in biotechnology, biology and medicine, in tests for acid-stable trypsin inhibitor of human urine in biological liquids. Bul.44/30.11.92

Dwg.0/0

L210 ANSWER 36 OF 67 USPATFULL

ACCESSION NUMBER: 91:40475 USPATFULL

Cytotoxic T lymphocte serine esterase and method for TITLE:

stimulation and inhibition

Pasternack, Mark S., Brookline, MA, United States INVENTOR(S):

Eisen, Herman S., Waban, MA, United States

Massachusetts Institute of Technology, Cambridge, MA, PATENT ASSIGNEE(S):

United States (U.S. corporation)

NUMBER KIND DATE ______ 19910521

PATENT INFORMATION: APPLICATION INFO.: US 5017489

19880822 (7) US 1988-234906

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Weimar, Elizabeth C. ASSISTANT EXAMINER: Patterson, Charles L. LEGAL REPRESENTATIVE: Kilpatrick & Cody NUMBER OF CLAIMS: 12

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 1025

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Antibodies, nucleic acid sequences, and methods for inhibition of lysis for a novel serine esterase produced by both murine and human

cytotoxic T lymphocytes. The serine esterase has an apparent molecular

weight of approximately 28,000-31,000, as determined by SDS gel electrophoresis under reducing conditions, and trypsin-like

activity. Inhibition of the esterase correlates with

inhibition of the cells' cytolytic activity. Specific inhibition of the serine esterase is useful as a method for immunosuppression as well as for the inhibition of cytolytic activity of T lymphocytes, both in vivo and in vitro. The genes encoding the murine and human serine

esterase are homologous.

L210 ANSWER 37 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1991-059025 [09] WPIDS

DOC. NO. CPI:

C1991-024917

TITLE:

New polypeptide derivs. of human tissue

plasminogen activator - used to treat thrombosiscid, prepd. from animal waste and legumes, using process heat

to destroy trypsin inhibitor.

DERWENT CLASS:

B04

INVENTOR(S):

BALDINGER, V; MULLERNEUM, M; SCHMIDT, M; SCHWARZ, M;

STRUBĖ, K H

PATENT ASSIGNEE(S):

(BADI) BASF AG

COUNTRY COUNT:

1

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG DE 3930099 A 19910221 (199109)*

APPLICATION DETAILS:

APPLICATION DATE PATENT NO KIND _____ DE 1989-3930099 19890909 DE 3930099 A

PRIORITY APPLN. INFO: DE 1989-3926039 19890807; DE 1989-3930099 19890909

AB DE 3930099 A UPAB: 19930928

(I) has one or two extra amino acids substd. or inserted in the 277-527th aminoacid region. Also claimed is a DNA sequence that codes for (I) and vectors contg. the appropriate gene sequence. The DNA sequence can be cloned from human uterine tissue, by isolating mRNA and transcribing into double-stranded cDNA. After inserting the cDNA into the conventional cloning vector pUC9, a cDNA library is built up. The cDNA clone can be isolated.

USE/ADVANTAGE - In the treatment of thrombolysis, (I) has an improved clotting specificity, longer half life, lower inhiBitOr binding and/or h%gher proteolytic activity than unmodified human tissue plasminogen activator.

0/9

L210 ANSWER 38 OF 67 MEDLINE

ACCESSION NUMBER: 91093294 MEDLINE

DOCUMENT NUMBER: 91093294 PubMed ID: 1985973

TITLE: Molecular cloning and sequence analysis of cDNAs coding for

guinea pig alpha 1-antiproteinases S and F and contrapsin.

AUTHOR: Suzuki Y; Yoshida K; Honda E; Sinohara H

CORPORATE SOURCE: Department of Biochemistry, School of Medicine, Kinki

University, Osaka, Japan.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Jan 15) 266 (2)

928-32.

Journal code: HIV; 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-M38571; GENBANK-M38572; GENBANK-M38573;

GENBANK-M57269; GENBANK-M57270; GENBANK-M57271; GENBANK-M57624; GENBANK-M60203; GENBANK-M60204; GENBANK-M60205; GENBANK-M60206; GENBANK-M62780;

GENBANK-M63262

ENTRY MONTH: 199102

ENTRY DATE: Entered STN: 19910322

Last Updated on STN: 19910322 Entered Medline: 19910212

The cDNAs encoding two isoforms, S (slow) and F (fast), of alpha AΒ 1-antiproteinase (also referred to as alpha 1-antitrypsin or alpha 1-proteinase inhibitor) as well as contrapsin were obtained by screening lambda gt11 cDNA library prepared fro inflamed guinea pig liver. The sequence analyses of these cDNAs and NH2-terminal peptides of the purified proteins revealed that both isoforms of alpha 1-antiproteinase consist of 405 amino acid residues including a signal peptide of 24 residues and that contrapsin consists of 410 amino acid residues with the same length of the signal peptide. Guinea pig contrapsin had 89, 88, 62, 42, and 41% homology to its own alpha 1-antiproteinases F and S, rat alpha 1-antiproteinase, mouse and rat contrapsins, respectively. This suggests that guinea pig contrapsin is not orthologous to mouse and rat contrapsins and that it developed from a much later duplication of alpha 1-antiproteinase gene after the guinea pig had diverged from the murine lineage. The available data suggest that the reactive site region of alpha 1-antiproteinase can be categorized into orthodox and unorthodox types: the former has P3-P'3 consensus sequence of Xaa-Pro-Met-Ser-Xaa-Pro, where Xaa is Leu, Ile, Val, or Met, while the latter, which occurs in species having multiple alpha

1-antiproteinase isoforms, has the sequence whose P1 Met has changed to other amino acids. Thus, the reactive site region of the orthodox type, which occurs in all seven mammals examined to date, is highly conserved. This is in marked contrast to the fact that the same region is hypervariable among the paralogous proteins belonging to the serpin superfamily.

L210 ANSWER 39 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1990-024493 [04] WPIDS

DOC. NO. CPI: C1990-010787

TITLE: Vampire bat glycosylated plasminogen activating protein - which needs fibrin co-factor to activate plasminogen has

greater selectively for fibrin-bound plasminogen than

T-pa.

DERWENT CLASS: B04 D16

INVENTOR(S): DAUGHERTY, B L; DIXON, R A F; DUONG, L T; FRIEDMAN, P A;

GARDELL, S J; JACOBS, J W; MARK, G E; JACOBS, J J

PATENT ASSIGNEE(S): (MERI) MERCK & CO INC; (SCHD) SCHERING AG

COUNTRY COUNT: 2

PATENT INFORMATION:

PAT	ENT NO	KIND	DATE		WEEK	LA	PG
EP	352119	A	19900	124	(199004) * EN	36
					GB GR IT		
PT	91236	Α	19900	208	(199009)	
ΑU	8938915	Α	19900	125	(199010)	
	8902976						
FI	8903500	Α	19900	121	(199018)	
	8905528						
DK	8903575	Α	19900	123	(199030)	
JP	02167075	A	19900	627	(199032)	
	352119						
	R: AT BE						NL SE
	91059				(199538		
	68923741						
	9503849						
	2076965						
	69054						
ИО	9700603	Α	19900	122	(199719)	
	100403						
	100406						
	2713467						31
	302954						
	5830849						
	134823						
	138997						
CA	1341090	С	20000	0829	(200051) EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 352119 ZA 8905528	A A	EP 1989-307411 ZA 1989-5528	19890720 19890720
JP 02167075	A	JP 1989-188673 EP 1989-307411	19890720 19890720
EP 352119 IL 91059	B1 A	IL 1989-91059	19890720
DE 68923741	E	DE 1989-623741 EP 1989-307411	19890720 19890720

FI	9503849	Α	Div ex	FI	1989-3500	19890719
				FI	1995-3849	19950815
ES	2076965	Т3		EP	1989-307411	19890720
ΙE	69054	В		IE	1989-2354	19890719
NO	9700603	Α	Div ex	NO	1989-2976	19890720
				NO	1997-603	19970210
FI	100403	В1		FI	1989-3500	19890719
FI	100406	В1	Div ex	FI	1989-3500	19890719
				FI	1995-3849	19950815
JP	2713467	B2		JP	1989-188673	19890720
NO	302954	В1		NO	1989-2976	19890720
US	5830849	Α	CIP of	US	1988-221697	19880720
			Cont of	US	1989-377221	19890713
			Cont of	US	1991-784102	19911028
			Cont of	US	1992-870170	19920416
				US	1995-467966	19950606
KR	134823	В1		KR	1997-39260	19970819
KR	138997	В1		KR	1989-10264	19890720
CA	1341090	С		CA	1989-606185	19890720

FILING DETAILS:

PAT	TENT NO	KIND			PAT	TENT NO	
DE	68923741	E	Based on	-	EP	352119	
ES	2076965	Т3	Based on		EP	352119	
FI	100403	B1	Previous	Publ.	FI	8903500	
FI	100406	B1	Previous	Publ.	FI	9503849	
JP	2713467	B2	Previous	Publ.	JP	02167075	
NO	302954	B1	Previous	Publ.	NO	8902976	

PRIORITY APPLN. INFO: US 1989-377221 19890713; US 1988-221697 19880720; US 1991-784102 19911028; US 1992-870170 19920416; US 1995-467966 19950606

AB EP 352119 A UPAB: 19950223

Purified glycosylated plasminogen activating protein (I) is new which: (a) requires a fibrin cofactor to activate plasminogen (PM); (b) catalyses lysis of plasma clots; and (c) is not inhibited by NaCl when in the presence of a fibrin clot; where mol. wt. of (I) by SDS-PAGE of deglycosylated fonus is <50 KD. (1) (I) with 90% homology with one of 4 sequences (given in specification), where (I) needs a fibrin cofactor in order to activate PM; (2) DNA sequences encoding 2 specified (I) sequences, and DNA

sequences with 90% homology with the other 2 specified

(I) sequences; (3) a replicable clotting vector contg. (2); (4) purificn. of (I) by: (a) homogenising submandibular glands from Desmodus rotundus vampire bats to form a mixt. and centrifuging; (b) clarifying and concentrating the supernatant; (c) applying vetentate to a

phosphocellulose cation exchange column and absorbing (I) to the column; (d) electing to obtain (I) fractions; (e) pooling and applying to an affinity column with immobilised Erythnira trypsin

inhibitor; (f) Factionating (I) by HPLC; and (g) sepg. (I) by
SDS-PAGE. (5) antibodies specifically reactive with (I); (6) glycosylated
PM activating fusion protein including residues 190-441 (see Fig.), and a
heavy chain sequence from t-PA, the protein having greater PM activating
activity than t-PA in presence of type-1 PM activating activity inhibitor;

and (7) mammalian and bacterial cells transfected with (3).

USE/ADVANTAGE - (I) has greater selectivity towards fibrin-bound PM, so may decrease severity and frequency of bleeding diathesis when used for thrombolytic therapy. (I)

0/12 Dwg.0/12

L210 ANSWER 40 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1990-024464 [04] WPIDS

DOC. NO. CPI: C1990-010772

TITLE: Human PSTI modified at arginine 42 and/or 44 - by substitution by glutamine and/or serine to allow

trypsin-inhibitory activity.

DERWENT CLASS: B04 D16

INVENTOR(S): KIKUCHI, N; SHIN, M; TERAOKA, H; YOSHIDA, N

PATENT ASSIGNEE(S): (SHIO) SHIONOGI & CO LTD; (SHIO) SHIONOGI SEIYAKU KK;

(SHIO) SHIONOGI PHARM CO LTD

COUNTRY COUNT: 18

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 352089	 А	19900124	(199004)	* EN	25
R: AT BE	CH I	E ES FR	GB GR IT	LI LU	NL SE
AU 8937978	Α	19900125	(199010)		
JP 02150282	Α	19900608	(199029)		
US 5122594	Α	19920616	(199227)		21
EP 352089	B1	19940216	(199407)	EN	31
R: AT BE	CH I	DE ES FR	GB GR IT	LI LU	NL SE
DE 68913090	E	19940324	(199413)		
ES 2062006	Т3	19941216	(199505)		
JP 07102137	B2	19951108	(199549)		20
CA 1339875	С	19980519	(199831)		
KR 9615745	B1	19961120	(199930)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 352089	A	EP 1989-307309	19890719
JP 02150282	A	JP 1988-255580	19881011
US 5122594	A	US 1989-379002	19890712
EP 352089	B1	EP 1989-307309	19890719
DE 68913090	E	DE 1989-613090	19890719
		EP 1989-307309	19890719
ES 2062006	Т3	EP 1989-307309	19890719
JP 07102137	B2	JP 1988-255580	19881011
CA 1339875	С	CA 1989-606044	19890718
KR 9615745	B1	KR 1989-10227	19890719

FILING DETAILS:

PAT	TENT NO	KIND			PAT	TENT NO
DE	68913090	E	Based	on	EP	352089
ES	2062006	Т3	Based	on	ΕP	352089
.TD	07102137	B2	Rased	on	JP	02150282

PRIORITY APPLN. INFO: JP 1988-181316 19880719; JP 1988-255580 19881011

AB EP 352089 A UPAB: 19930928

Modified human PSTI (pancreatic secretory trypsin inhibitor (I)) is disclosed where Arg (42) and/or (44) from the N-terminus of the natural human PSTI amino acid sequence are replaced with

Glu and/or Ser. Also disclosed are: (1) (I) where Arg (42) or (44) are replaced with Glu and/or Ser, respectively; (2) (I) where one of Arg (42) or Arg (44) is/are replaced by Glu or Ser, (II); (3) (I) where Arg (42) is replaced by Glu; (4) (I) where Arg (44) is replaced by Ser; (5) (I) having the sequence shown in fig. 1 or fig. 2; (6) Any **DNA** sequence encoding the above; (7) Use of the above (I) as a therapeutic trypsin inhibitor.

USE - (I) allows a sustained trypsin inhibition effect useful in the clinical treatment of acute paucreatitis.
0/9

L210 ANSWER 41 OF 67 MEDLINE

ACCESSION NUMBER: 90148955 MEDLINE

DOCUMENT NUMBER: 90148955 PubMed ID: 2302382

TITLE: Molecular cloning and primary structure of rat alpha

1-antitrypsin.

AUTHOR: Chao S; Chai K X; Chao L; Chao J

CORPORATE SOURCE: Department of Pharmacology and Biochemistry, Medical

University of South Carolina, Charleston 29425.

CONTRACT NUMBER: HL29397 (NHLBI)

SOURCE: BIOCHEMISTRY, (1990 Jan 16) 29 (2) 323-9.

Journal code: AOG; 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M32247

ENTRY MONTH: 199003

ENTRY DATE: Entered STN: 19900601

Last Updated on STN: 19900601 Entered Medline: 19900326

A cDNA clone encoding rat alpha 1-antitrypsin has been isolated from a lambda gt-11 rat liver cDNA library using an antigen-overlay immunoscreening method. The nucleotide sequence of this cDNA clone is 1306 base pairs in length and has a coding region of 1224 base pairs which can be translated into an alpha 1-antitrypsin precursor protein consisting of 408 amino acid residues. The cDNA sequence contains a termination codon, TAA, at position 1162 and a polyadenylation signal sequence, AATAAT, at position 1212. The calculated molecular weight of the translated mature protein is 43,700 with 387 amino acid residues; this differs from purified rat alpha 1-antitrypsin's apparent molecular weight of 54,000 because of glycosylation. Five potential glycosylation sites were identified on the basis of the cDNA sequence. The translated mature protein sequence from the cDNA clone matches completely with the N-terminal 33 amino acids of purified rat alpha 1-antitrypsin, which has an N-terminal Glu. The cDNA encoding rat alpha 1-antitrypsin shares 70% and 80% sequence identity with its human and mouse counterparts, respectively. The reactive center sequence of rat alpha 1-antitrypsin is highly conserved with respect to human alpha 1-antitrypsin, both having Met-Ser at the P1 and P1' residues. Genomic Southern blot analysis yielded a simple banding pattern, suggesting that the rat alpha 1-antitrypsin gene is single-copy. Northern blot analysis using the cDNA probe showed that rat alpha 1-antitrypsin is expressed at high levels in the liver and at low levels in the submandibular gland and the lung. (ABSTRACT TRUNCATED AT 250 WORDS)

L210 ANSWER 42 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:38264 CAPLUS

DOCUMENT NUMBER: 114:38264

TITLE: Amino acid sequence elucidation of human

acrosin-trypsin inhibitor (HUSI-II) reveals that

R. Mitra; 09/667,380

Kazal-type proteinase inhibitors are structurally related to .beta.-subunits of glycoprotein hormones Fink, Edwin; Hehlein-Fink, Christa; Eulitz, Manfred Dep. Clin. Chem. Clin. Biochem., Univ. Munich, Munich,

CORPORATE SOURCE: Dep. Clin. Chem. Clin. D-8000, Fed. Rep. Ger.

SOURCE: FEBS Lett. (1990), 270(1-2), 222-4

CODEN: FEBLAL; ISSN: 0014-5793

DOCUMENT TYPE: Journal LANGUAGE: English

AUTHOR(S):

The amino acid sequence of the acrosin-trypsin inhibitor HUSI-II from human seminal plasma is presented which unequivocally identifies HUSI-II as being of Kazal-type. In addn., the HUSI-II sequence shows a striking similarity to the middle part of glycoprotein hormone .beta.-subunits thus revealing a hitherto unknown structural and evolutionary relation between Kazal-type inhibitors and glycoprotein hormones.

L210 ANSWER 43 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1989-025643 [04] WPIDS

DOC. NO. CPI: C1989-011390

TITLE: Human pancreatic secretory trypsin

inhibitor - obtd. by recombinant DNA techniques
and free from other proteins of human origin.

DERWENT CLASS: B04 D16

INVENTOR(S): KANAMORI, T; MOCHIDA, E; NOBUHARA, M; OGINO, H

PATENT ASSIGNEE(S): (MOCH) MOCHIDA PHARM CO LTD; (MORP) MORISHITA PHARM CO

 $_{
m LTD}$

COUNTRY COUNT: 13

PATENT INFORMATION:

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 300459	A	EP 1988-111704	19880720
JP 01027473	A	JP 1987-184556	19870723

PRIORITY APPLN. INFO: JP 1987-184556 19870723

AB EP 300459 A UPAB: 19930923

A human pancreatic secretory trypsin inhibitor (PSTI) free of other proteins of human origin is claimed. Also claimed is a vector replicable in E. coli comprising (a) a DNA sequence encoding the human PSTI and (b) a promoter, an SD sequence and a DNA sequence encoding a signal peptide, which function within E. coli. Also claimed are transformants of E. coli transformed by the vector.

A DNA sequence encoding the human PSTI may be obtd. by extracting a genomic DNA of a human cell, by synthesising a human PSTI cDNA from mRNA extd. from a human cell or by designing the DNA sequence encoding the human PSTI on the basis of the amino acid sequence of any of the 4 isoinhibitors and chemically synthesising the DNA. Prefd. E. coli strains for expressing the protein are lipoprotein-deleted mutant strains.

USE/ADVANTAGE - The human PSTI is free of any contaminants associated

with the purified human PSTI from natural sources. It may be used for the prodn. of monoclonal antibody and the diagnosis of various PSTI-associated diseases.

0/8

L210 ANSWER 44 OF 67 MEDLINE

ACCESSION NUMBER: 90114211 MEDLINE

DOCUMENT NUMBER: 90114211 PubMed ID: 2608068

TITLE: Organization of the human corticosteroid binding globulin

gene and analysis of its 5'-flanking region.

AUTHOR: Underhill D A; Hammond G L

CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of

Western Ontario, Victoria Hospital, London, Canada. MOLECULAR ENDOCRINOLOGY, (1989 Sep) 3 (9) 1448-54.

SOURCE: MOLECULAR ENDOCRINOLOGY, (1989 Sep) 3 (9) 14

Journal code: NGZ; 8801431. ISSN: 0888-8809.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199002

ENTRY DATE: Entered STN: 19900328

Last Updated on STN: 19900328 Entered Medline: 19900215

The structure of the human corticosteroid binding globulin (CBG) gene has AΒ been determined, and restriction endonuclease maps of human placental DNA and cloned genomic DNA indicate that CBG is encoded by a single gene. The transcription unit for hepatic CBG mRNA comprises five exons distributed over approximately 19 kilobases (kb), and nuclease protection and primer extension studies using human liver RNA demonstrate that the first exon spans 70 base pairs (bp). Typical of many eukaryotic promoters, sequences that resemble TATA and CAAT-box motifs are centered 28 bp and 73 bp upstream from the origin of transcription, respectively. In addition, six highly conserved sequence elements, responsible for efficient, liver-specific expression of the mouse albumin gene, are located within the first 200 bp of the 5'-flanking region. Further analysis of a region (500 bp) immediately 5' of the transcription start site, however, failed to reveal sequences that might correspond to known steroid hormone response elements. When compared to other serine protease inhibitor genes, the organization of the human CBG gene is most closely related to the human alpha 1-proteinase inhibitor and alpha 1-antichymotrypsin genes. It would therefore appear that these proteins are derived from a common ancestral gene, and this supports the concept that they may be functionally related.

L210 ANSWER 45 OF 67 MEDLINE

ACCESSION NUMBER: 89325681 MEDLINE

DOCUMENT NUMBER: 89325681 PubMed ID: 2568950

TITLE: Cloning of the pig aminopeptidase N gene. Identification of

possible regulatory elements and the exon distribution in

relation to the membrane-spanning region.

AUTHOR: Olsen J; Sjostrom H; Noren O

CORPORATE SOURCE: Department of Biochemistry C, Panum Institute, University

of Copenhagen, Denmark.

SOURCE: FEBS LETTERS, (1989 Jul 17) 251 (1-2) 275-81.

Journal code: EUH; 0155157. ISSN: 0014-5793.

PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198908

ENTRY DATE:

Entered STN: 19900309

Last Updated on STN: 20000303 Entered Medline: 19890829

We have isolated four lambda-phages covering the complete pig AΒ aminopeptidase N/CD13 gene. The sequence of 2.85 kbp encompasses 1.18 kbp of the 5' upstream region and 1.67 kbp of the structural gene. In the promoter region we find a TATA box and potential binding sites for CTF-1/NF-1 and AP-2. By sequence comparisons we have found three domains showing similarity to promoter regions of the genes encoding human alpha 1-antitrypsin and human intestinal alkaline phosphatase. The gene sequence includes the first three exons and two introns. It shows that a single exon encodes the cytoplasmic tail, the membrane anchor and the junctional peptide.

L210 ANSWER 46 OF 67 USPATFULL

ACCESSION NUMBER:

88:68916 USPATFULL

TITLE:

Process for concentrating and separating trypsin inhibitor and kallidinogenase

in human urine

INVENTOR(S):

Yuki, Yoshikazu, Kobe, Japan

Nakanishi, Koichiro, Ashiya, Japan Hiratani, Hajime, Sennan, Japan

PATENT ASSIGNEE(S):

Japan Chemical Research Co., Ltd., Kobe, Japan

(non-U.S. corporation)

NUMBER KIND DATE US 4780209 19881025 US 1987-104634 19871002

PATENT INFORMATION: APPLICATION INFO.:

US 1987-104634

(7)

RELATED APPLN. INFO.:

Continuation of Ser. No. US 1986-870083, filed on 3 Jun

1986, now abandoned

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Therkorn, Ernest G.

LEGAL REPRESENTATIVE: Bryan, Cave, McPheeters & McRoberts

NUMBER OF CLAIMS:

11

EXEMPLARY CLAIM: NUMBER OF DRAWINGS:

1 Drawing Figure(s); 1 Drawing Page(s)

392 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Two components, trypsin and kallidinogenase, in human urine are concentrated simultaneously by allowing human urine at neutral pH, collecting bubbles thus formed to obtain the concentrate of the two components, adjusting the concentrate to weak acidity, contacting the acidified concentrate with chitosan to allow the two components to be adsorbed onto chitosan, eluting the components from the adsorbent with aqueous ammonia solution, and neutralizing and heating the eluate at about 60.degree. C. for about 10 hours to make the eluate virus-free, followed by separating the components from the eluate.

L210 ANSWER 47 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER:

1988-133245 [19] WPIDS

DOC. NO. CPI:

C1988-059638

TITLE:

Human pancreatic secretory trypsin

inhibitors - used to prevent and treat diseases resulting in auto digestion of pancreatic tissue.

DERWENT CLASS:

B04 D16

INVENTOR(S):

BANDYOPADH, P; EISENBERG, S; KOHNO, T; THOMPSON, R

PATENT ASSIGNEE(S):

(SYND) SYNERGEN BIOLOGICAL INC

COUNTRY COUNT:

T.Z

PG

PATENT INFORMATION: DAMENIO NO

PAT	FN.I.	NO	1	KIND	D.F	4.LE		W	SEK			LΑ	P	3									
WO	880	 3171	- - L	 А	19	9880	505	5 (:	198	819)) *	EN	3 :	9									
	RW:																						
	W:	AΤ	ΑU	BB	ВG	BR	CH	DE	DK	FI	GB	HU	JP	ΚP	KR	LK	LU	MC	MG	MW	$N\Gamma$	ИО	RO
		SD	SE	SU																			
	878						520																
DK	880	3442	2	Α	19	9886	0623	3 (:	198	846))												
NO	880	2843	3	Α	19	9881	1017	7 (:	198	847))												
EP	329	693		Α	19	9890	0830	(198	935))	EN											
	R:	ΑT	BE	CH	DE	FR	GB	IT	LI	LU	NL	SE											
JP	025	0102	27	W	19	9900	0412	2 (:	199	021)												
EP	329	693		Α4	19	9893	1115	5 (199	508)												

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803171	A	WO 1987-US2585	19871009
EP 329693	A	EP 1987-907369	19871009
JP 02501027	W	JP 1987-506869	19871009
EP 329693	A4	EP 1987-907369	

MEEK

PRIORITY APPLN. INFO: US 1986-924991 19861030

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WO 8803171 A UPAB: 19930923

A novel human pancreatic secretory trypsin inhibitor (HPSTI) comprises a protein possessing at least one active site with the ability to inhibit proteases, where the inhibitor is homologous to that isolatable from human pancreatic tissues and where the inhibitor is produced using recombinant DNA methods.

USE/ADVANTAGE - The HPSTI and analogues prepd. by recombinant DNA methods enable improved research into the prevention and treatment of diseases resulting in the autodigestion of pancreatic tissue and are used to prevent the trypsin-catalysed activation of pancreatic proteolytic zymogens. The HPSTI and some analogues are biologically equiv. to HPSTI isolatable from human pancreatic tissues and juices. Other analogues are capable of inhibiting proteolytic enzymes other than trypsin to prevent destruction of various tissues, e.g. elastase which has been implicated in a causative role in emphysema. 0/3

L210 ANSWER 48 OF 67 MEDLINE

ACCESSION NUMBER: 88122641 MEDLINE

PubMed ID: 2893291 88122641 DOCUMENT NUMBER:

Novel precursor of Alzheimer's disease amyloid protein TITLE:

shows protease inhibitory activity.

Kitaguchi N; Takahashi Y; Tokushima Y; Shiojiri S; Ito H AUTHOR: Life Science Research Laboratories, Asahi Chemical Industry CORPORATE SOURCE:

Co. Ltd., Shizuoka, Japan.

NATURE, (1988 Feb 11) 331 (6156) 530-2. SOURCE:

Journal code: NSC; 0410462. ISSN: 0028-0836.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals GENBANK-X06981 OTHER SOURCE:

ENTRY MONTH: 198803 ENTRY DATE: Entered STN: 19900308

Last Updated on STN: 19980206 Entered Medline: 19880317

Alzheimer's disease is characterized by cerebral deposits of amyloid AB beta-protein (AP) as senile plaque core and vascular amyloid, and a complementary DNA encoding a precursor of this protein (APP) has been cloned from human brain. From a cDNA library of a human glioblastoma cell line, we have isolated a cDNA identical to that previously reported, together with a new cDNA which contains a 225-nucleotide insert. The sequence of the 56 amino acids at the N-terminal of the protein deduced from this insert is highly homologous to the basic trypsin inhibitor family, and the lysate from COS-1 cells transfected with the longer APP cDNA showed an increased inhibition of trypsin activity. Partial sequencing of the genomic DNA encoding APP showed that the 225 nucleotides are located in two exons. At least three messenger RNA species, apparently transcribed from a single APP gene by alternative splicing, were found in human brain. We suggest that protease inhibition by the longer APP(s) could be related to aberrant APP catabolism.

L210 ANSWER 49 OF 67 MEDLINE

ACCESSION NUMBER: 88314108 MEDLINE

DOCUMENT NUMBER: 88314108 PubMed ID: 2842251

TITLE: Molecular structure and sequence homology of a gene related

to alpha 1-antitrypsin in the human genome.

AUTHOR: Bao J J; Reed-Fourquet L; Sifers R N; Kidd V J; Woo S L

CORPORATE SOURCE: Howard Hughes Medical Institute, Baylor College of

Medicine, Houston, Texas 77030.

CONTRACT NUMBER: HL07343 (NHLBI)

HL27509 (NHLBI) HL37188 (NHLBI)

SOURCE: GENOMICS, (1988 Feb) 2 (2) 165-73.

Journal code: GEN; 8800135. ISSN: 0888-7543.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-J03044; GENBANK-M19684; GENBANK-M19685

ENTRY MONTH: 198810

ENTRY DATE: Entered STN: 19900308

Last Updated on STN: 19970203 Entered Medline: 19881011

A 7.7-kb EcoRI genomic DNA fragment highly homologous to the human alpha AΒ 1-antitrypsin (AAT) gene has been cloned. This antitrypsin-related sequence is physically linked to the authentic AAT gene and both are present in a single cosmid clone. Nucleotide sequencing of the AAT-related genomic fragment demonstrated extensive homology with the authentic AAT gene in the introns as well as in the exons. The conservation of all RNA splice sites and lack of internal termination codons in the exonic regions suggest that it may not be a classical pseudogene. If expressed, it could result in a protein of 420 amino acid residues exhibiting a 70% overall homology with human alpha 1-antitrypsin. The signal peptide sequence is well conserved in the related gene, but the active site for protease inhibition of Met-Ser in alpha 1-antitrypsin has been changed to Trp-Ser. These data suggest that the putative protein encoded by the AAT-related gene is a secretory serine protease inhibitor with an altered substrate specificity. Interestingly, even the intronic regions in the related gene exhibit a 65% overall nucleotide sequence homology with those of the authentic AAT gene. These results suggest that the AAT-related gene is derived from a recent duplication of the authentic AAT gene and represents a new member of the serine protease inhibitor superfamily.

L210 ANSWER 50 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1986-169458 [26] WPIDS

CROSS REFERENCE:

1986-169441 [26]; 1988-227612 [32]; 1999-166640 [14]; 1999-346413 [29]; 2000-678667 [63]; 2001-637974 [62];

2002-121475 [13]

DOC. NO. CPI:

C1986-072812

TITLE:

New synthetic DNA sequences for

directing microbial synthesis - for prodn. of single poly peptide chain serine protease inhibitor having leukocyte

elastase and trypsin inhibitory sites.

DERWENT CLASS:

B04 D16

INVENTOR (S):

OHLSSON, K; THOMPSON, R C; BANDYOPADH, P K; EISENBERG, S

P; STETLER, G L

PATENT ASSIGNEE(S):

(SYND) SYNERGEN BIOLOGICAL INC

COUNTRY COUNT:

19

PATENT INFORMATION:

PATENT NO F	CIND DATE	WEEK	LA	PG
WO 8603519	A 19860	519 (198626)	* EN	62
RW: AT BE	CH DE FR (B IT LU NL	SE	
W: AU DK	FI HU JP I	CR NO		
ES 8700691	A 19870	L16 (198711)		
ZA 8509363	A 198703	305 (198721)		
JP 62501262	W 19870	521 (198726)		
JP 2672088	B2 19971	LO5 (1997 <mark>4</mark> 9)		30

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8603519	A	WO 1985-US2385	19851204
ES 8700691	Α	ES 1985-549630	19851205
ZA 8509363	A	ZA 1985-9363	19851206
JP 62501262	W	JP 1986-500018	19851204
JP 2672088	B2	WO 1985-US2385	19851204
		JP 1986-500018	19851204

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 2672088	B2 Previous I Based on	Publ. JP 62501262 WO 8603519

19851204; US 1984-678822 PRIORITY APPLN. INFO: WO 1985-US2385

19841206

AΒ 8603519 A UPAB: 20020429

(1) Synthetic DNA sequence capable of directing microbial synthesis of a single polypeptide chain serine protease inhibitor (I) having at least one active site possessing serine protease inhibitor activity is new. (I) has good homology to the native serin protease inhibitor isolated from parotid secretions. (2) Translational coupler having the nucleotide sequence of formula (II) is new. TAA CGA GGC GCA AAA AAT GAA AAA GAC AGC TAT CGC GAT CAA GGA GAA ATA AAT G (II) USE/ADVANTAGE - The DNA sequence directs synthesis of (I), which is believed to have at least 2 active sites, one exhibiting leukocyte elastase inhibiting properties and the other exhibiting inhibitory activity against

trypsin. (I) has good resistance to heat and acids and it is resistant to proteolytic degradation by a variety of proteolytic enzymes. It is also thermodynamically stable under the conditions normally encountered extracellularly in the mammalian body. Denatured forms of (I) can also form the disulphide bonds and can form the no-covalent interactions necessary to assume an active tertiary structure in the absence of biochemical stimulus. (I) differs greatly from other known leukocyte elastase inhibitors. It can be prepd. from the DNA sequence in quantities and amts. sufficient for economic use.

L210 ANSWER 51 OF 67 MEDLINE

ACCESSION NUMBER: 86120356 MEDLINE

DOCUMENT NUMBER: 86120356 PubMed ID: 3003690

TITLE: A new member of the plasma protease inhibitor gene family.

AUTHOR: Ragg H

SOURCE: NUCLEIC ACIDS RESEARCH, (1986 Jan 24) 14 (2) 1073-88.

Journal code: O8L; 0411011. ISSN: 0305-1048.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-X03498

ENTRY MONTH: 198603

ENTRY DATE: Entered STN: 19900321

Last Updated on STN: 19900321 Entered Medline: 19860321

AB A 2.1-kb cDNA clone representing a new member of the protease inhibitor family was isolated from a human liver cDNA library. The inhibitor, named human Leuserpin 2 (hLS2), comprises 480 amino acids and contains a leucine residue at its putative reactive center. HLS2 is about 25-28% homologous to three human members of the plasma protease inhibitor family: antithrombin III, alpha 1-antitrypsin and alpha 1-antichymotrypsin. A comparison with published partial amino acid sequences shows that hLS2 is closely related to the thrombin inhibitor heparin cofactor II.

L210 ANSWER 52 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:418949 CAPLUS

DOCUMENT NUMBER: 103:18949

TITLE: Human inter-.alpha.-trypsin inhibitor: localization

of the Kunitz-type domains in the N-terminal part of the molecule and their release by a trypsin-like

proteinase

AUTHOR(S): Reisinger, Peter; Hochstrasser, Karl; Albrecht, Gerd

J.; Lempart, Kathrin; Salier, Jean Philippe

CORPORATE SOURCE: Klin. Poliklin. Hals-, Nasen- Ohrenkranke, Univ.

Muenchen, Munich, D-8000/70, Fed. Rep. Ger.

SOURCE: Biol. Chem. Hoppe-Seyler (1985), 366(5), 479-83

CODEN: BCHSEI

DOCUMENT TYPE: Journal LANGUAGE: English

The N-terminal amino acid sequence of human inter-.alpha.-trypsin inhibitor (ITI) is identical with that of the acid-stable human 30-kilodalton inhibitors (HI-30) from urine and serum and with those released from inter-.alpha.-trypsin inhibitor by trypsin or chymotrypsin. Serum HI-30 and HI-30 released by trypsin differ from the urinary inhibitor by an addnl. C-terminal arginine residue. Compared to these 2 inhibitors, the inhibitor released by chymotryptic proteolysis is elongated C-terminally by an addnl. phenylalanine residue. HI-30 thus appears to be the N-terminus of the inter-.alpha.-trypsin inhibitor,

released from this inhibitor in vivo by cleavage of the Arg123-Phe124 peptide bond by trypsinlike proteinases.

L210 ANSWER 53 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:518718 CAPLUS

DOCUMENT NUMBER: 103:118718

Studies on the protease inhibitors in lung cancer TITLE:

tissue. I. Purification of urinary trypsin

inhibitor-like inhibitor from human lung cancer tissue

Okumichi, Tsuneo AUTHOR(S):

Sch. Med., Hiroshima Univ., Hiroshima, 734, Japan CORPORATE SOURCE:

Hiroshima Daigaku Igaku Zasshi (1985), 33(1), 1-16 SOURCE:

CODEN: HDIZAB; ISSN: 0018-2087

Journal DOCUMENT TYPE: Japanese LANGUAGE:

Trypsin-inhibitory activity was significantly higher in exts. from human lung cancer tissue than in that from normal lung tissue. The antigenicity of the inhibitor in the lung cancer tissue was the same as that of urinary trypsin inhibitor as detd. by double immunodiffusion,

immunoelectrophoresis, and neutralization with rabbit anti-(urinary trypsin inhibitor) IgG. The mol. wt. of the lung cancer trypsin inhibitor was .apprx.67,000 in gel filtration. The inhibitor was sepd. into 2 bands

with mol. wt. of 43,000 and 20,000 on SDS-polyacrylamide gel

electrophoresis (SDS-PAGE). From 1 g of lung cancer tissue, 20-60 .mu.g of the inhibitor, with a specific activity of 2,000 units/mg protein was obtained by the SDS-PAGE method. The lung cancer trypsin inhibitor markedly inhibited trypsin, chymotrypsin, and kallikrein, and weakly inhibited plasmin, but it did not inhibit urokinase, thrombin, or collagenase.

L210 ANSWER 54 OF 67 CAPLUS COPYRIGHT 2002 ACS

1984:402886 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 101:2886

Isolation of two novel proteinase inhibitors from TITLE:

hemolymph of silkworm larva, Bombyx mori. Comparison

with human serum proteinase inhibitors

Sasaki, Takuji; Kobayashi, Kazuto AUTHOR (S):

Sch. Agric., Nagoya Univ., Nagoya, 464, Japan CORPORATE SOURCE: J. Biochem. (Tokyo) (1984), 95(4), 1009-17 SOURCE:

CODEN: JOBIAO; ISSN: 0021-924X

DOCUMENT TYPE: Journal

English LANGUAGE:

Two protein proteinase inhibitors, antitrypsin and antichymotrypsin, were isolated from the hemolymph of silkworm larva, B. mori, using conventional gel filtration and ion-exchange chromatog. techniques. They had similar physicochem. properties, e.g. mol. wt. (42,000 for antitrypsin and 43,000 for antichymotrypsin), amino acid compn., and CD spectrum. Further comparison of these characteristics with human serum inhibitors, .alpha.-1-proteinase inhibitor and .alpha.-1-antichymotrypsin, suggested the resemblance of silkworm and human inhibitors. The N-terminal sequences were not, however, homologous to each other, and antiserum against each silkworm inhibitor only formed a precipitin line with its own antigen. Differences in minute parts of the inhibitors are indicated.

L210 ANSWER 55 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:120615 CAPLUS

DOCUMENT NUMBER:

98:120615

TITLE:

The human .alpha.1-antitrypsin gene: its sequence

homology and structural comparison with the

chicken ovalbumin gene

AUTHOR (S):

Woo, Savio L. C.; Chandra, T.; Kidd, Vincent J.; Long,

George L.; Kurachi, Kotoku; Davie, Earl W.

CORPORATE SOURCE:

Howard Hughes Med. Inst. Lab., Baylor Coll. Med.,

Houston, TX, 77030, USA

SOURCE:

UCLA Symp. Mol. Cell. Biol. (1982), 26(Gene Regul.),

55-64

CODEN: USCBDO

DOCUMENT TYPE:

Journal English

LANGUAGE:

Genomic .alpha.-antitrypsin [9035-81-8] DNA clones were isolated from a human DNA library with an .alpha.1-antitrypsin cDNA clone from baboon as hybridization probe; the mol. structure of the

human gene was examd. by hybridization with .alpha.-1

antitrypsin-specifying mRNA of baboon and electron microscopy of hybrids.

The screening of 2 .times. 106 plaques from the human genomic DNA library yielded 16 independent phage isolates which originated from 4 independent clones, designated .alpha.AT135, .alpha.AT35, .alpha.AT80, and .alpha.AT101. Hybridization of the human genomic DNA and baboon mRNA showed that the gene contained exon regions I, II, III, and IV of

0.71, 0.33, 0.13, and 0.27 kilobases and introns A, B, and C of 1.45, 1.15, and 0.8 kilobases. The 9.6-kilobase EcoRI DNA fragment contg. the human gene was subcloned into the EcoRI site of plasmid pBR322;

the resulting plasmid, pAT 9.6, was examd. by restriction mapping and Southern hybridization. The presence of 4 exons and 3 introns within the gene was confirmed. The human .alpha.1-antitrypsin gene shared significant sequence homol. with the chick ovalbumin gene, but the no., positions, and sizes of the intervening sequences differed. The

evolutionary origin of the 2 genes is discussed.

L210 ANSWER 56 OF 67 USPATFULL

ACCESSION NUMBER:

75:54506 USPATFULL

TITLE:

Protease inhibitor from horse urine Singh, Kartar, Beaconsfield, Canada

INVENTOR(S): PATENT ASSIGNEE(S):

Ayerst, McKenna and Harrison Ltd., Montreal, Canada

(non-U.S. corporation)

KIND DATE NUMBER ______

PATENT INFORMATION:

US 3912704

19751014

APPLICATION INFO .:

19740513

RELATED APPLN. INFO.:

US 1974-469180 Continuation-in-part of Ser. No. US 1972-251168, filed

on 8 May 1972, now abandoned

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Schain, Howard E.

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

LINE COUNT:

548

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A protease inhibitor isolated from horse urine particularly active against trypsin, chymotrypsin and plasmin which differs from a similar inhibitor isolated from human urine in having a different isoelectric point, different staining properties, and about twice the trypsin-inhibiting activity of the latter, and a process for isolating the said protease inhibitor from horse

MEDLINE

urine.

MEDLINE L210 ANSWER 57 OF 67

ACCESSION NUMBER: 74147535

DOCUMENT NUMBER: 74147535 PubMed ID: 4274689

TITLE: Treatment of chronic urticaria with a proteinase

(kallikrein) inhibitor.

AUTHOR: Berova N; Petkov I; Andreev V C

SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1974 Apr) 90 (4) 431-4.

Journal code: AWO; 0004041. ISSN: 0007-0963.

PUB. COUNTRY: ENGLAND: United Kingdom

(CLINICAL TRIAL)

(CONTROLLED CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 197406

ENTRY DATE: Entered STN: 19900310

Last Updated on STN: 20000303 Entered Medline: 19740619

L210 ANSWER 58 OF 67 MEDLINE

ACCESSION NUMBER: 74157850 MEDLINE

DOCUMENT NUMBER: 74157850 PubMed ID: 4545256

TITLE: Interaction of human serum proteinase inhibitors with

proteolytic enzymes of animal, plant, and bacterial origin.

AUTHOR: Sasaki M; Yamamoto H; Iida S

SOURCE: JOURNAL OF BIOCHEMISTRY, (1974 Jan) 75 (1) 171-7.

Journal code: HIF; 0376600. ISSN: 0021-924X.

PUB. COUNTRY: Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 197407

ENTRY DATE: Entered STN: 19900310

Last Updated on STN: 19900310 Entered Medline: 19740705

L210 ANSWER 59 OF 67 MEDLINE

ACCESSION NUMBER: 74091289 MEDLINE

DOCUMENT NUMBER: 74091289 PubMed ID: 4130044

TITLE: Serum protein profiles in thermal burns. II. Protease

inhibitors, complement factors, and c-reactive protein.

AUTHOR: Daniels J C; Larson D L; Abston S; Ritzmann S E SOURCE: JOURNAL OF TRAUMA, (1974 Feb) 14 (2) 153-62.

Journal code: KAF; 0376373. ISSN: 0022-5282.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals ENTRY MONTH: 197404

ENTRY DATE: Entered STN: 19900310

Last Updated on STN: 19900310

Entered Medline: 19740402

L210 ANSWER 60 OF 67 MEDLINE

ACCESSION NUMBER: 73000150 MEDLINE

DOCUMENT NUMBER: 73000150 PubMed ID: 4262591

TITLE: Human skin proteases.
AUTHOR: Fraki J E; Hopsu-Havu V K

SOURCE: ARCHIV FUR DERMATOLOGISCHE FORSCHUNG, (1972) 243 (3)

153-63.

Journal code: 6X5; 7512588. ISSN: 0003-9187.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

197211

ENTRY DATE:

Entered STN: 19900310

Last Updated on STN: 19900310 Entered Medline: 19721108

L210 ANSWER 61 OF 67 MEDLINE

ACCESSION NUMBER:

72112495 MEDLINE

DOCUMENT NUMBER:

72112495 PubMed ID: 4536746

TITLE:

[Comparison of the effects of proteinase inhibitors antilysin, contrycal and trasylol on trypsin and

chymotrypsin activity in man].

Srovnani ucinku proteinazovych inhibitoru Antilysinu, Contrykalu a Trasylolu na trypsinovou a chymotrypsinovou

aktivitu cloveka.

AUTHOR:

Malis F; Fric P; Slezak Z

SOURCE:

CESKOSLOVENSKA GASTROENTEROLOGIE A VYZIVA, (1972 Jan) 26

(1) 12-7.

Journal code: CTK; 0402356. ISSN: 0009-0565.

PUB. COUNTRY:

Czechoslovakia

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

Czech

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

197204

ENTRY DATE:

Entered STN: 19900310

Last Updated on STN: 19900310 Entered Medline: 19720428

L210 ANSWER 62 OF 67

ACCESSION NUMBER: 71234464

MEDLINE

MEDLINE

DOCUMENT NUMBER:

71234464 PubMed ID: 4253726

TITLE:

Studies of kallikrein inhibitors in potatoes. II. Effect of

potato kallikrein inhibitors on various kallikreins and

other proteases.

AUTHOR:

Hojima Y; Moriya H; Moriwaki C

SOURCE:

JOURNAL OF BIOCHEMISTRY, (1971 Jun) 69 (6) 1027-32.

Journal code: HIF; 0376600. ISSN: 0021-924X.

PUB. COUNTRY:

Japan

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

197108

ENTRY DATE:

Entered STN: 19900101

Last Updated on STN: 20000303 Entered Medline: 19710821

L210 ANSWER 63 OF 67

MEDLINE

ACCESSION NUMBER:

72025013 MEDLINE

DOCUMENT NUMBER:

72025013 PubMed ID: 4939580

TITLE:

[Physiopathology and clinical picture of hereditary

antiproteinase deficiency syndromes]. Pathophysiologie und Klinik hereditarer

Antiproteinasen-Mangelsyndrome.

AUTHOR:

Duck H J

SOURCE:

ZEITSCHRIFT FUR DIE GESAMTE INNERE MEDIZIN UND IHRE GRENZGEBIETE, (1971 Jul 15) 26 (14) 445-51. Ref: 107

Journal code: XUY; 21730470R. ISSN: 0044-2542.

PUB. COUNTRY:

GERMANY, EAST: German Democratic Republic

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE:

German

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

197112

ENTRY DATE:

Entered STN: 19900310

Last Updated on STN: 19900310 Entered Medline: 19711230

MEDLINE L210 ANSWER 64 OF 67

ACCESSION NUMBER:

71130810 MEDLINE

DOCUMENT NUMBER:

71130810 PubMed ID: 5313313

TITLE:

The kinin-system of human plasma. I. Isolation of a low

molecular weight activator of prekallikrein.

AUTHOR:

Movat H Z; Poon M C; Takeuchi Y

SOURCE:

INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY,

(1971) 40 (1) 89-112.

Journal code: GP9; 0404561. ISSN: 0020-5915.

PUB. COUNTRY:

Switzerland

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

197104

ENTRY DATE:

Entered STN: 19900101

Last Updated on STN: 20000303 Entered Medline: 19710420

L210 ANSWER 65 OF 67

MEDLINE

ACCESSION NUMBER:

70182221 MEDLINE

DOCUMENT NUMBER:

70182221 PubMed ID: 5309810

TITLE:

[Influence of Trasylol on the effect of various proteases on erythrocytes].

Uber den Einfluss von Trasylol bezuglich der Wirkung von

verschiedenen Proteasen auf Erythrocyten.

AUTHOR:

Uhlenbruck G; Wintzer G

SOURCE:

KLINISCHE WOCHENSCHRIFT, (1969 Jun 15) 47 (12) 673-5.

Journal code: KWH; 2985205R. ISSN: 0023-2173. GERMANY, WEST: Germany, Federal Republic of

PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

German

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

197006

ENTRY DATE:

Entered STN: 19900101

Last Updated on STN: 20000303 Entered Medline: 19700624

L210 ANSWER 66 OF 67

MEDLINE

ACCESSION NUMBER:

68090073° MEDLINE

DOCUMENT NUMBER:

68090073 PubMed ID: 4229180

TITLE:

In vitro and in vivo studies with trasylol, an anticoagulant and a fibrinolytic inhibitor.

AUTHOR:

SOURCE:

Dubber A H; McNicol G P; Uttley D; Douglas A S

BRITISH JOURNAL OF HAEMATOLOGY, (1968 Jan) 14 (1) 31-49. Journal code: AXC; 0372544. ISSN: 0007-1048.

PUB. COUNTRY:

ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

196802

ENTRY DATE:

Entered STN: 19900101

Last Updated on STN: 19970203

Entered Medline: 19680214

L210 ANSWER 67 OF 67 MEDLINE

ACCESSION NUMBER: 68099678 MEDLINE

DOCUMENT NUMBER: 68099678 PubMed ID: 5299789

TITLE: [On the mechanism of the effect of various inhibitors of

fibrinolysis].

K mechanismu ucinku nekterych inhibitoru fibrinolyzy.

AUTHOR: Donner L; Houskova J

SOURCE: SBORNIK LEKARSKY, (1967) 69 (11) 343-51.

Journal code: UAW; 0025770. ISSN: 0036-5327.

PUB. COUNTRY: Czechoslovakia

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Czech

FILE SEGMENT: Priority Journals

ENTRY MONTH: 196802

ENTRY DATE: Entered STN: 19900101

Last Updated on STN: 19900101 Entered Medline: 19680226